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JOURNAL OF ANATOMY

THE RIPE HUMAN GRAAFIAN FOLLICLE, TOGETHER WITH SOME SUGGESTIONS AS TO ITS MODE OF RUPTURE

BY ARTHUR THOMSON,

Professor of Human Anatomy, University of Oxford

For the purposes of this paper the ripe Graafian follicle is defined as one which, from its superficial position, its size, and the thickness of the wall separating it from the ovarian surface, there is reason to believe is fast approaching the time at which rupture may take place. Added to this, must necessarily be considered the condition of the contained ovum. If evidence is forthcoming that the ovum is passing through, or has passed, the maturation stage, such is confirmatory proof that so far as the contents of the follicle are concerned they are ready for discharge. If, as not unfrequently happens, the ovum exhibits indications of degenerative changes, these must be taken into account in any estimate that may be formed regarding the normal appearance of the follicle.

Admitting that coincident with its approach to the surface of the ovary, the Graafian follicle enlarges, what are we to regard as the normal measures of its size? One can readily understand that there may be, and are, considerable variations in the dimensions of a follicle which in other respects fulfils the conditions which are to be regarded as indications of its ripeness.

Size of ripe Graafian Follicle. When reference is made to the various British and foreign text-books, it will be found that there is great disparity in the measures given. The dimensions recorded range from 2 mm. to 20 mm., the average size being about 15 mm. in diameter. In my experience this latter figure is much too high. In the specimens I have examined of follicles exceeding a diameter of 5 mm. I have either failed to find a contained ovum or when it was met with, it proved to be in a degenerated condition.

For these reasons a certain amount of caution is necessary before accepting the figures usually quoted, for mere naked eye inspection of the ovary, on section, may be misleading, since though the follicles exposed may be of considerable size, there is no proof that their contents are normal.

Nagel ((23), p. 44), to whom deference must be paid as a reliable observer, says that the follicle may attain a diameter of 10–20 mm. before it ruptures, and that no limits can be fixed to its growth within these figures; the test is whether the follicle contains a normal ovum. Testut ((31), p. 696), on the other

hand, is much more conservative in his estimate; he describes the follicle as usually measuring between 2 and 3 mm. or more, occasionally as much as 9 mm. As will be noticed, his upper limit falls below the lower value given by Nagel.

If it be that the larger figures, viz. 15 to 20 mm., are of common occurrence, it follows that the ovary in which such a follicle is found must present a remarkable appearance, since the size of the ovary itself is usually recorded as about 30 mm. in length, so that the presence of so large a follicle in its substance would very materially affect the surrounding tissue, and would greatly alter the external appearance of the organ.

It is possible that immediately prior to its rupture the Graafian follicle may undergo a sudden and rapid increase in its size, but so far, in the material at my disposal, I have not come across any follicles of the larger dimensions given, which in other respects could be regarded as normal.

Possibly deductions as to the size of the ripe follicle prior to its rupture have been made from the appearance displayed by the presence of corpora lutea in different stages of development, but in regard to this it may be observed, that we are without information as to the rapidity and extent of the changes that may ensue within the follicle immediately after its rupture.

In the accompanying table the results are given, so far as the size of the follicle is concerned, as observed in the material at my disposal.

Table I

Size of ripe Graafian Follicles containing Normal Ova

The measures are given in millimetres.

Specimen		Diameters	Distance from Surface
453 A	35*	1·63 × 2·00 × 1·96	0·3
01	122	4·53 × 3·14 × 4·90	0·3
453 B	14*	2·62 × 1·56 × 2·54	0·34
02	106	0·79 × 0·80 × 0·62	0·36
01	95	4·59 × 3·16 × 4·82	0·56
U 3	27	3·20 × 3·08 × 5·20	0·6
380	98**	1·47 × 1·84 × 2·80	0·88
453 A	3**	1·39 × 1·66 × 2·34	1·00
02	67	0·71 × 1·18 × 2·06	1·04
01	14	2·90 × 2·58 × 2·09	1·16
453 F	34	0·98 × 0·56 × 1·20	1·28
453 F	20	1·42 × 1·70 × 1·56	2·6
453 F	30	1·37 × 0·96 × 1·20	2·6

The specimens in this table are arranged in order of the thickness of the wall which separates the Graafian follicle from the surface of the ovary. Generally speaking, those with the thinnest wall are the larger follicles, though this is not an invariable rule, as may be seen from an inspection of the table. It would therefore appear that there is considerable variation in the size of the follicle independent of its proximity to the surface.

In specimens 453 B 14 and 453 A 35 (marked *) the contained ova, after

examination, have been pronounced mature. In specimens **453 A 3** and **380 98** (marked **), the contained ova are in the process of maturation.

Apparently the healthy Graafian follicle tends to be spherical, as if well filled. In cases where it is irregular in shape and angular in form the contents are generally found to be in a degenerated condition.

If the examples given in the above table are to be regarded as ripe for rupture, their relatively small size suggests that they are in a more or less quiescent condition, and that prior to their rupture they will undergo a sudden and more or less rapid increase in their bulk when the appropriate occasion arises. This is a matter which will be dealt with later in the paper.

Position of Cumulus

Another point on which there is much conflict of opinion, in the published accounts, is the position within the Graafian follicle of the cumulus or discus proligerus surrounding the ovum.

Nagel ((23), p. 57) very definitely states that "in man, and, as it seems, in most mammals (Waldeyer, Frey, Henle) the cumulus always has this position on the medial wall of the follicle, somewhat more to one side or the other of the middle line, and consequently always opposite the stigma (the point where the follicle ruptures)." This view is acquiesced in and followed by Poirier ((25), p. 695, vol. III.), Tigerstedt (32), and Piersol ((24), p. 1989).

McMurrich ((18), p. 19) qualifies it somewhat by stating that the discus is found "at one point *usually* on the surface nearest the centre of the ovary."

H. N. Martin ((20), p. 73) takes a diametrically opposite view, assigning a position to the cumulus usually corresponding to that "nearest the surface of the ovary."

A. Flint ((9), p. 759) expresses the opinion that "the situation of the discus proligerus is not invariable; sometimes it is in the most superficial and sometimes it is in the deepest part of the Graafian follicle."

Most authors maintain a discreet silence on the point, whilst J. H. Raymond ((26), p. 627) accepts the view of Böhm and Davidoff ((3), p. 352) to the effect that the discus proligerus with the contained ovum ultimately comes to lie free in the liquor folliculi, a change which is brought about by the softening of the cells forming the pedicle of the discus.

As the outcome of my own observations I feel justified in saying that the position of the cumulus or discus proligerus is not always on the deep wall of the follicle opposite the stigma, as stated by Nagel and others, but that in fact it may be frequently met with on the most superficial aspect of the follicle, i.e. that nearest the surface of the ovary, and consequently close to the stigma or point of rupture. Indeed, the position of the cumulus appears to be determined by no known law, and its occurrence on any part of the circumference of the follicle may be observed.

The view almost universally accepted, is that the discus proligerus remains throughout the growth of the follicle adherent to the cells of the stratum

granulosum through the medium of a pedicle which may vary considerably in appearance, in some cases being long and attenuated, in others short and wide. The appearance represented under the microscope will vary much according to the plane of section, and any satisfactory elucidation of the subject is only possible after the careful examination and reconstruction of serial sections.

It frequently happens that a single section, or, it may be, a small series of sections, would give support to the view that the discus proligerus with the contained ovum lay free in the liquor folliculi. On more extensive examination, however, so far as my own experience goes, these specimens can always be traced so as to reveal a connexion with the cells of the stratum granulosum. Such an observation, however, does not necessarily contravert the view taken by Böhm and Davidoff, for it is possible, as will be hereafter explained, that the cumulus and ovum may be found floating in the liquor folliculi, having acquired that position by a means other than that described by these authors, viz. the division of the pedicle.

The advantage of having the ovum and discus proligerus floating fairly free in the liquor folliculi is at once apparent when we come to discuss the mode and manner of the discharge of the ovum when the Graafian follicle ruptures.

It is obvious that the position of the cumulus must stand in some distinct relation to the mechanism which determines the escape of the ovum from the follicle.

If one accepts the view that the cumulus is always situated on that side of the follicle which lies farthest from the surface of the ovary, it becomes at once difficult to explain how it is possible, by any increase of pressure in the fluid contained within the antrum folliculi, for the ovum to be expelled through an aperture which lies on the opposite side to that on which it is placed. It seems more probable that the fluid pressure being equally exerted in all directions, is rather likely to force the ovum more firmly against the wall on which it rests. Hence the obvious advantage of a more superficial position as claimed by Martin (*loc. cit.*), for there the ovum resting on or in relation to the weakened wall of the follicle (stigma), where the rupture is about to take place, will naturally be expelled through the orifice made in the wall of the theca against which it lies, by the bursting pressure exerted by the liquor folliculi. Such an explanation seems feasible, and would be one way of explaining the escape of the ovum in those cases in which the cumulus is superficial in position. But the question naturally arises, is it the normal way?

In cysts which enlarge through the increasing amount of their fluid contents, there is a tendency towards the production of marked flattening of the cellular contents which line their more resisting envelopes. If this be the case, we would expect to find the cells of the stratum granulosum lining the interior of the follicle thinned and compressed, an appearance which we do not see; the absence of such a condition is probably to be accounted for on the supposition that these cells are really part and parcel of the liquor folliculi, forming

as it were a superficial layer of cells bathed in and surrounding the liquor folliculi, overlying, but not intimately attached to, the "basal membrane" or "external limiting membrane" of some authors (see Robinson (27) pp. 311 and 319) which lines the inner surface of the internal theca. It is on this layer that the pressure exercised by the contents of the follicle is apparently exerted, else, were the cells of the stratum granulosum a constituent part of the wall of the follicle, we would expect these cells, as already stated, to exhibit indications of the result of pressure. Reference will be made later to this basal membrane, meanwhile it will be sufficient to suggest that possibly there is a lymph space in association with it.

What holds good of the cells of the stratum granulosum must also apply equally to the cells of the cumulus. It would be natural to expect that in cases where the cumulus has a broad base and an absence of pedicle, the follicular cells of which it is composed would react to such pressure as may be exerted on them, were it not that they form a constituent part of the fluid and semi-fluid contents of the follicle. What is true of these cells would also apply to the ovum which they surround, consequently we are entitled to assume that all the contents of the follicle within the basal membrane are subject to an equality of pressure, whatever that pressure may be. For the present the consideration of this subject is postponed until certain other details of the Graafian follicle have been considered. Meanwhile I here place on record my own observations as to the position of the cumulus within the follicle.

In 15 Graafian follicles which might be accounted as "ripe," and having normal contents, the cumulus or discus proligerus was in seven cases situated superficially, that is towards the ovarian surface. In two instances it lay deep within the follicle, the term "deep" being here employed to indicate that the cumulus was placed on the wall of the follicle farthest removed from the surface of the ovary. In six follicles the cumulus lay to one or other side of the follicle, intermediate in position between the superficial and deep positions above indicated.

In 10 Graafian follicles either containing degenerate contents, or not so advanced in growth, the cumulus was situated six times superficially, twice laterally, and in two cases deeply.

These records are too few from which to deduce any reliable data, but are sufficient to contravert Nagel's statement, for out of 25 Graafian follicles the cumulus occupies a superficial position in 13 cases, or about 50 per cent. whereas it only occurs in the "deep" position, that accounted as normal by Nagel, in four instances or 16 per cent.

Liquor Folliculi

Concerning the manner of the production of the liquor folliculi there is much divergence of opinion. The question at issue is whether the liquor folliculi is of intercellular or intracellular origin.

Scattered among the follicular epithelium, contained within the Graafian

follicle, are certain structures called the bodies of Call and Exner (4). These have been variously interpreted, by some as vacuolated cells (the "epithelial vacuoles" of Flemming ((8), p. 378)), by others as intercellular collections.

The prevalent ideas with regard to the origin of the liquor folliculi may be briefly stated as follows. Nagel ((23), p. 54) regards it as formed partly by transudation from the vessels surrounding the follicle, partly by disintegration of the large follicular cells (the "bodies of Call and Exner" or the "epithelial vacuoles" of Flemming), whose protoplasm swells, finally to be completely broken up, the nucleus at the same time crumbling away and finally breaking up.

On the other hand C. Honoré ((14), p. 537), from his researches on the rabbit, states that the stratum granulosum secretes the liquor folliculi just as the epithelium of the tubes of the kidney secretes urine. He explains the presence and appearance of the bodies of Call and Exner as follows. A certain number of the cells of the stratum granulosum group themselves radially and *secrete* a substance at first homogeneous. This central substance later becomes a reticulum, and increases in size with the growth of the follicle; the reticulum becomes finer, and a kind of peripheral membrane appears, at the same time the radial arrangement of the surrounding cells becomes less evident. The staining of these bodies in follicles of different sizes shews that their chemical constitution is modified by age.

My own observations on this subject may best be explained by a series of microphotographs, which I venture to think illustrate the successive stages of the process.

The feature which enables the observer to recognise them consists in the arrangement, in radial fashion, of the follicle cells disposed around them. This appearance is so characteristic that Call and Exner suggested that they were of the nature of ova, and that the arrangement of the cells surrounding them was comparable to the corona radiata encircling the ovum.

Within the area circumscribed by this radial formation of the follicular cells, in a typical example, there is a mass of variable size, often of a more or less clear, homogeneous matter, reacting to some stains in a selective way, but generally presenting appearances which correspond in tint and density with the reaction to the same stain of the coagulum in the antrum folliculi. The nature of the material occupying the centres of these radially arranged follicular cells has been variously interpreted. By some, these "bodies" have been regarded as the product of the liquefaction of the protoplasm of the follicular cells (Nagel (22), p. 381; Waldeyer (34), p. 38). Bernhart considered them of a fatty nature, but this view was combated by Bischoff, who held that they failed to refract the light sufficiently to justify this assumption. Flemming describes them as vacuoles of epithelial origin. C. Honoré regards them as having an intercellular origin and as being due to the accumulation of the products of the special activity of the radially arranged follicular cells around them.

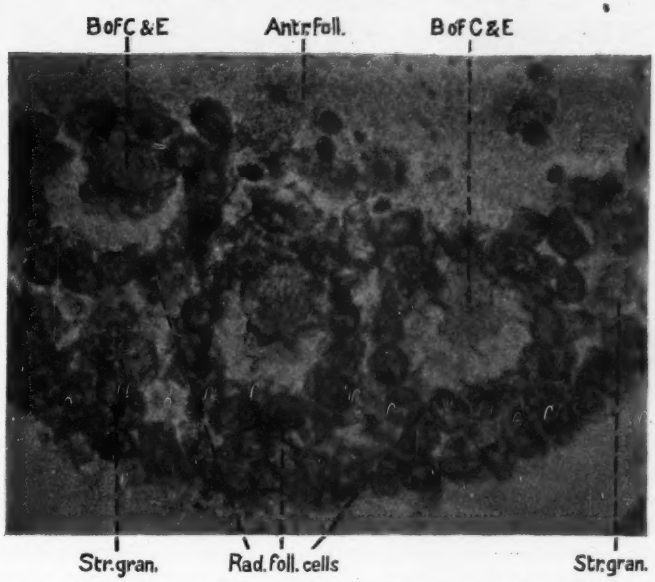

Fig. 1. Shewing bodies of Call and Exner (B. of C. and E.) surrounded by radial arrangement of follicular cells (*Rad. foll. cells*) in the stratum granulosum (*str. gran.*) of a human Graafian follicle. × 900 diameters. *Antr. foll.* antrum folliculi. Specimen 280 G. 5.

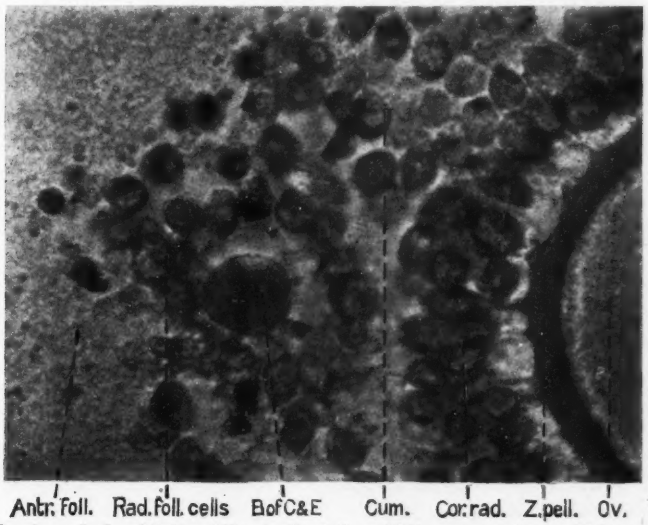

Fig. 2. Shewing a body of Call and Exner (B. of C. and E.) surrounded by radial arrangement of follicular cells (*Rad. foll. cells*) in the cumulus (*cum.*) of a human Graafian follicle. × 900. *Ov.* ovum.—*Z. pell.* zona pellucida.—*Cor. rad.* corona radiata.—*Antr. foll.* antrum folliculi. Specimen 280 G. 4.

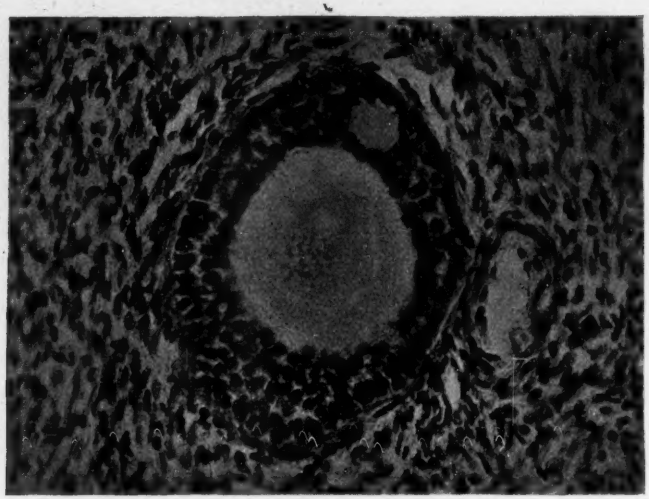

Fig. 3. Ovum within the stroma of the ovary surrounded by follicular cells. As yet there is no antrum folliculi. Near 1 of the watch dial there is a body of Call and Exner surrounded by a corona of follicular cells, within which the structure presents a homogeneous appearance. ×400. Specimen O. 2. 59. 4.

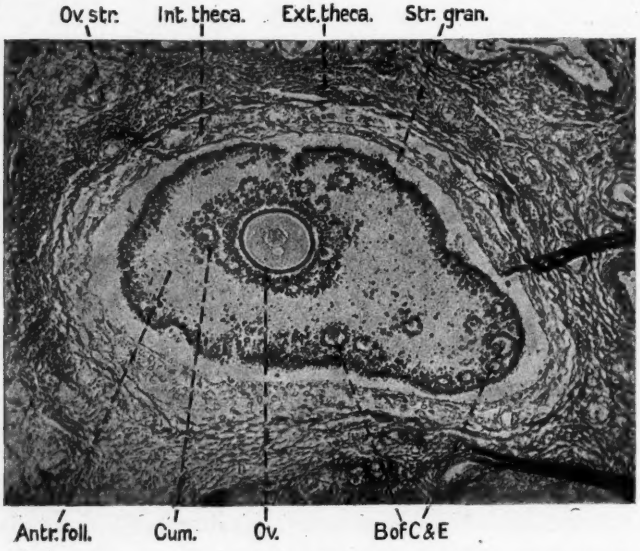

Fig. 4. Section of a human Graafian follicle containing a maturing ovum. *Ov. str.* ovarian stroma; *Int. theca*, internal theca; *ext. theca*, external theca; *str. gran.* stratum granulosum; *antr. foll.* antrum folliculi; *cum.* cumulus, with bodies of Call and Exner therein; *ov.* ovum; surrounded by zona pellucida and corona radiata. B. of C. and E., Bodies of Call and Exner in the stratum granulosum. ×100. Specimen 280. G. 2.

In attempting an elucidation of these various views it will be necessary to draw attention first to the stage at which these bodies make their earliest appearance, and the manner of their distribution.

Fig. 3 represents the appearance of one of these bodies as seen in a Graafian follicle in which there is as yet no antrum folliculi. In the specimen shewn, the body of Call and Exner is of large size as contrasted with others which occur in the serial sections of the same follicle, and its contents react to the stain (iron haematoxylin and Van Giesen) in such a manner as to be coloured a deep orange. It may be noted that in follicles in which an antrum folliculi occurs, under the same staining reagents the enclosed coagulum is usually tinted yellow. The same relation is seen in specimens stained with Mallory's connective tissue stain, both coagulum and "bodies" are coloured blue, the latter much more deeply. This circumstance would suggest that the liquor folliculi is of the same or similar nature as the matter contained in the bodies of Call and Exner, though possibly more dilute.

The question of size, to which reference has been already made, is a matter of some importance, as will presently be noted, as having a bearing on the manner of formation of these bodies.

In regard to their distribution. As stated above, they occur in follicles prior to the formation of the antrum folliculi, and I have seen evidences of what I took to be their genesis in follicles as early as the double-layered stage of the follicular epithelium. Subsequent to the appearance of the antrum folliculi, they are met with equally amongst those parts of the follicular epithelium which are ultimately to become the stratum granulosum, and in the cumulus, as shewn in fig. 4.

When, however, by the increase in the size of the antrum folliculi, the stratum granulosum becomes much thinned, then we find their occurrence in that layer much less frequent, until in advanced stages of the growth of the follicle they cease to be met with in the stratum granulosum altogether.

Not so, however, in the region of the cumulus, for here, immediately around the ovum and towards the basal part of the cumulus, they may be seen in follicles which are to be regarded as near approaching rupture, to judge by the thinness of the superficial wall and the mature condition of the oöcyte.

Meanwhile it may be noted that these so-called bodies of Call and Exner, in different stages of their development, exhibit very different appearances.

I am fortunate in being able to reproduce a microphotograph of the appearances displayed in the basal region of the cumulus where that structure becomes continuous with the stratum granulosum. Here within the same field certain appearances are to be noted which very definitely suggest that these bodies are the result of changes actually taking place in single follicular cells, or, it may be, in groups of such cells (fig. 5).

Fig. 6 is a view shewing in the centre of the field a follicular cell which is remarkable on account of its size and appearance.

Enclosed within a definite cell wall the cytoplasm appears uniformly granu-

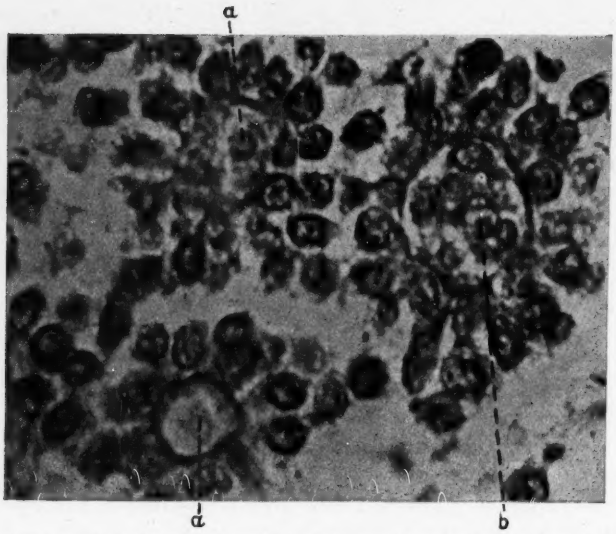

Fig. 5. Section through the base of the cumulus of a human Graafian follicle shewing three bodies of Call and Exner (*a*, *a*, *b*). Two of these (*a*, *a*) are seen to be formed from single follicular cells, whilst *b* exhibits their origin from a group of follicular cells. × 900. Specimen 280. 12. 5.

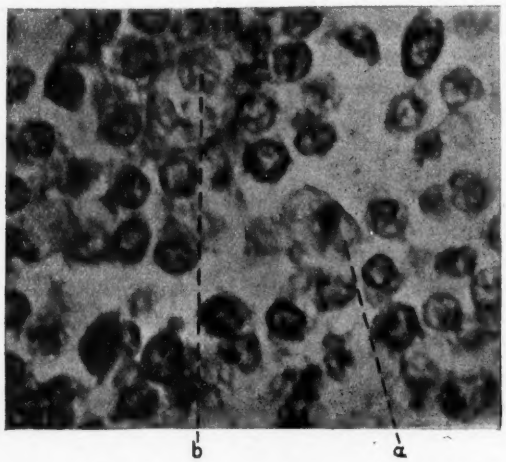

Fig. 6. Section through the follicular epithelium shewing *a* an enlarged follicular cell prior to its being surrounded by a corona of contiguous follicular cells. At *b* a similar follicular cell is seen in process of being so surrounded. × 900. Specimen 453 A. 4. 5.

lar, and stains somewhat more deeply than that of the surrounding cells; within this the nucleus shews up as a darker mass with no clearly defined nuclear membrane such as is so characteristic of the surrounding cells, and the chromatin granules are no longer isolated, but appear to be diffused through the nuclear protoplasm (karyoplasm) in such a way as to impart a darker tint to the whole nuclear substance, evidently a stage in the ultimate dissolution of that structure.

In fig. 7 a further stage is exhibited. Here there is distinct evidence of a vacuolation of the cytoplasm taking place within the cell membrane, while the nucleus becomes less distinct and seems to be more diffuse. At the same time, as will be seen in the figure, the surrounding follicular cells, by the increasing

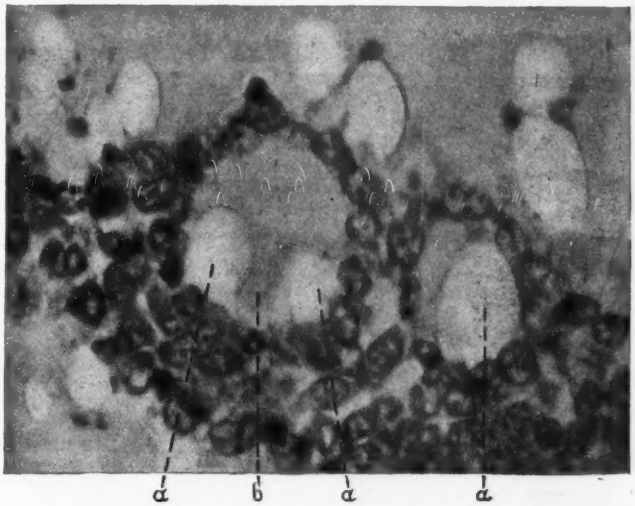

Fig. 7. Section shewing vacuolation of cells composing bodies of Call and Exner, *a*, *a*, *a*. At *b* the nucleus of one of them is disappearing. × 900. Specimen 280. 16. 5.

expansion of the central cell undergoing these changes, arrange themselves in radial fashion, as would naturally be expected under the circumstances. In the same field another such body is seen enclosed in typical fashion by the characteristic radial formation of the surrounding follicular cells, though here a large vacuole occupies the major part of the cell and the nucleus has disappeared.

The occurrence of the vacuolation seems to vary in different examples; in many this phenomenon does not occur till after the nucleus is completely dissipated within the substance of the cell, so that the central mass produced would seem to form a more or less homogeneous, seemingly solid, clearly staining material, occupying the centre of the radial formation of the follicular cells. The change in the subsequent appearance of this substance is effected through

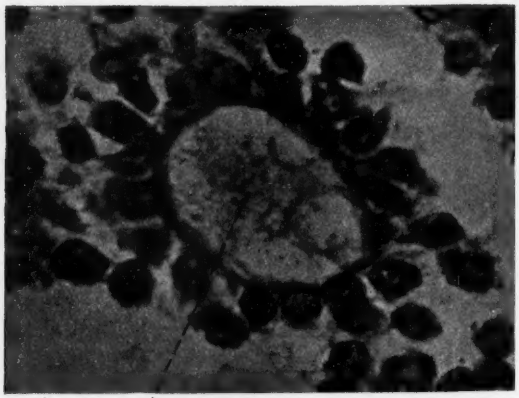

Fig. 8. Section shewing the body of Call and Exner now reduced to the form of a reticulum by the vacuolation of its substance. Around the vesicle so formed the contiguous follicular cells are grouped in coronal fashion. ×900. Specimen 453 A. 4. 5.

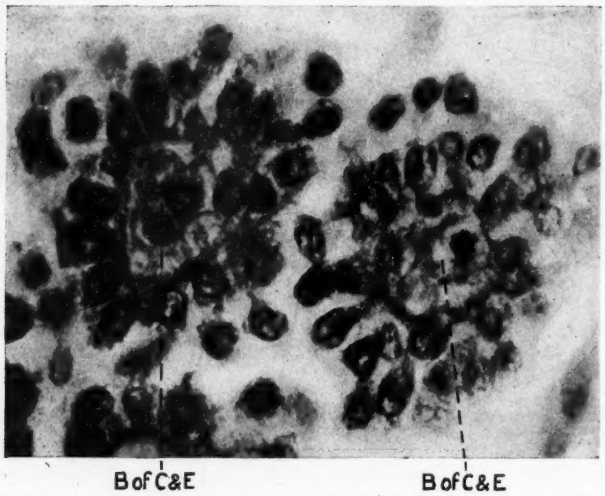

Fig. 9. Section shewing how the bodies of Call and Exner (B. of C. and E.) may be compounded of a number of follicular cells. ×900. Specimen 453 A. 4. 5.

the appearance either at the side of, or within it, of vacuoles of different sizes. In the first instance these spaces may be small and few, in which case the appearance presented is that of a coarse reticulum. In other cases the central mass may be transformed into a fine reticulum by the presence of a number of vacuoles which break it up in a more effective way, as seen in fig. 8.

Hitherto we have assumed that these appearances are the result of the changes induced in one follicular cell, but there is evidence that groups of cells may be agglutinated together, becoming, so to speak, encapsuled to form the centre of a radial formation, thereby greatly increasing the size of the so-called "body of Call and Exner." Fig. 9 represents this appearance.

The individual cells of these groups appear to undergo the same changes as those noted in the single cells already referred to, resulting in the fusion

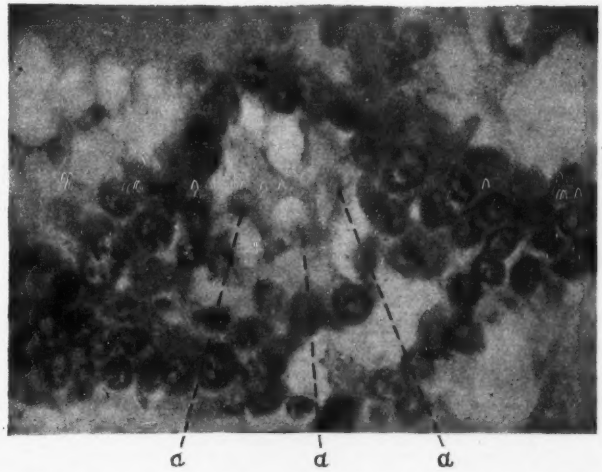

Fig. 10. Section of a body of Call and Exner vacuolated and shewing the disappearing nuclei, *a, a, a,* of some of the cells of which it is compounded. × 900. Specimen 280. 12. 5.

of their products, and displaying this difference, that the size of the resulting body is considerably larger, and the reticulum more complex.

A further proof of this is seen in fig. 10, where there is distinct evidence of the presence of nuclear structures within the resulting reticulum.

The microphotographs here reproduced make it clear that the bodies of Call and Exner can in no sense be regarded as due to the accumulation of the products of the special activity of the radially arranged follicular cells around them, as suggested by Honoré, but must be interpreted as the result of changes in a follicular cell or group of cells, whereby modifications are induced in their molecular structure, leading to the production of certain materials at different periods of their dissolution, and ultimately resulting in a liquefaction of the

bulk of their contents, which, together with a residual stroma, contributes to the increase in the amount of the liquor folliculi.

In this respect my observations lead me to support the view advanced by Nagel and others. There can, I think, be little doubt but that the radial arrangement of the surrounding follicular cells is a purely mechanical result, and that the so-called bodies of Call and Exner are merely to be considered as foci of the processes which ultimately result in the breaking down of the primarily compact mass of follicular cells, coincident with the production of an antrum folliculi and the subsequent distension of that cavity with fluid.

In this way the major part of the follicular cells disappears. As to how they are replaced or multiply, we have the evidence of Flemming ((8), p. 376 and pl. XIX, figs. 32–34), who describes the frequent occurrence of karyokinetic figures in the cells of the stratum granulosum of the cat and the rabbit, and of Harz ((12) p. 374) who records mitosis in the follicular cells of the mouse, whilst Nagel ((22) p. 379, pl. XXI, fig. 14) refers to it as demonstrated in the human female.

In Professor A. Robinson's memoir (27) I note the occurrence of mitotic division as exhibited in his beautiful series of microphotographs (see fig. 58, pl. X).

It follows that subsequent to the disappearance of the bulk of the follicular cells, only a thin layer of cells, often only a single row in thickness, is left lining the inner surface of the internal theca, and over-spreading the external limiting membrane. This much reduced layer constitutes the stratum granulosum.

The only other situation in which the follicular cells appear to persist is in the region of the cumulus, where in nearly all advanced Graafian follicles they remain as a stalk or pedicle to the mass of cells which contains the ovum.

In these situations the follicular cells which may subsequently undergo liquefaction, if this term may be employed, are not bedded in a compact mass of surrounding cells, but often lie in such a position that one part of their surface is only covered by a single layer of follicular cells, or may lie free in the wall of the antrum folliculi. The first of these conditions is represented in fig. 11, where in the stratum granulosum the body comparable to that of Call and Exner is represented by the cyst-like formation, the wall of which, directed to the antrum folliculi, is formed of a thinned and spread-out layer of follicular cells.

Fig. 12 shews the changes presented by a follicular cell superficially placed, i.e. one of the cells lining the antrum folliculi. Here, within a vacuole, the contained nucleus is exhibited undergoing evident dissolution. Similar changes are also represented in fig. 13, in which case the change in the appearance of the nucleus within the vacuole is less marked.

It would seem, in some cases, that the nuclear elements do not entirely disappear, a fact which would account for the presence in the liquor folliculi of the numerous nuclear-like bodies not unfrequently met with.

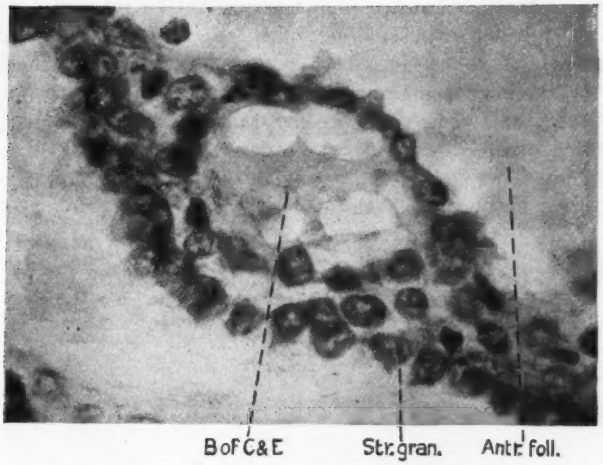

Fig. 11. Section of a body of Call and Exner in the stratum granulosum (*str. gran.*) separated from the antrum folliculi (*antr. foll.*) by but a single layer of follicular cells. ×900. Specimen 280. 12. 5.

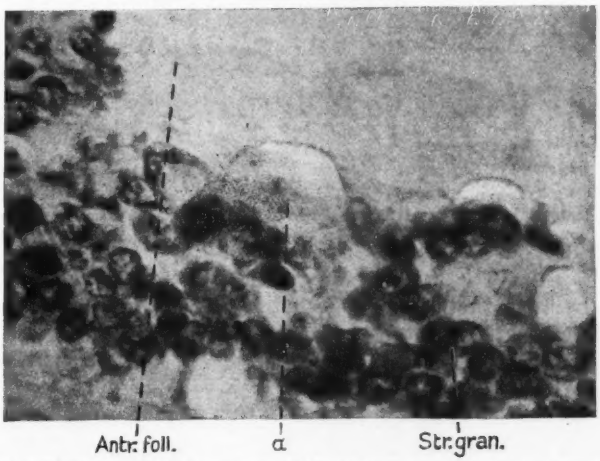

Fig. 12. Section shewing a follicular cell, *a*, of the stratum granulosum (*str. gran.*) undergoing dissolution. The nucleus is seen in an altered condition surrounded by a vacuolated space which may either be an artefact of the nature of a retraction cavity or may contain fluid of a different chemical constitution from that contained within the antrum folliculi (*antr. foll.*) which is seen in the form of a coagulum. ×900. Specimen 280. 16. 5.

In considering the changes in the follicular epithelium coincident with the appearance and expansion of the antrum folliculi, a staining reaction which is by no means infrequent must be here referred to. This consists in a marked difference with which some of these follicular cells react to the same stain, or combination of stains. It is best seen in the specimens which have been subjected to the influence of some such reagent as Mallory's connective tissue stain, whereby some of the cells become stained of a pink or a yellow colour, as contrasted with others (the majority) which exhibit a blue tint, an occurrence which would suggest that some of the cells were undergoing a change in their chemical constitution.

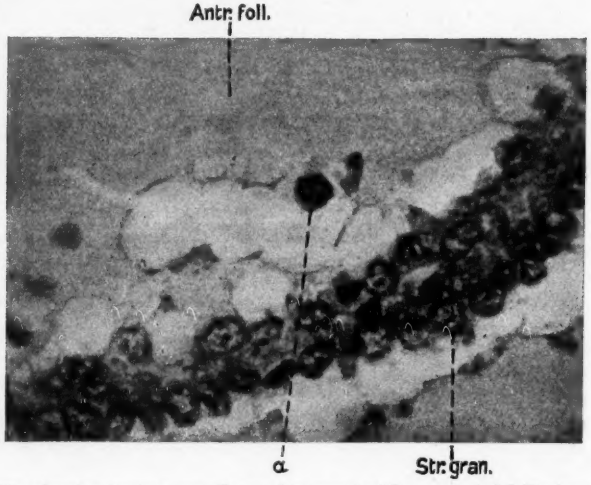

Fig. 13. Section shewing stratum granulosum (*str. gran.*) with a separated follicular cell (*a*) lying within a vacuolated space within the coagulum occupying the antrum folliculi (*antr. foll.*). The separated follicular cell (*a*) does not as yet present any appearance of undergoing change. The vacuole around it may be an artefact or due to the vital activity of the cell (*a*). ×900. Specimen 280. 14. 4.

It has been said that the cells of the stratum granulosum lining the interior of the follicle and resting on the membrana limitans externa which separates them from the inner surface of the internal theca, although often reduced to a single row of cubical cells, yet exhibit no appearance of flattening or compression, such as would be due to the result of pressure from within; for this reason these cells must be regarded as a constituent part of the contained liquid contents of the follicle, the pressure exercised by which is supported by the internal theca overlain by the membrana limitans externa.

Another matter to which attention must be incidentally directed is the fact that the stratum granulosum is exceedingly prone to separate from the inner theca of the follicle. In this connexion the observations of Robinson ((27), p. 320) on the ovarian follicles of the ferret are of interest. After pointing out

that Wagener, Schottländer, and Limon regard the membrana limitans externa as a connective tissue structure, whilst Waldeyer and Nagel believe that it is formed by the follicular cells, the latter asserting that it is similar at first to the oölemma, Robinson proceeds to point out that in the ferret, the membrana limitans externa does not react to stains in the same way as does the oölemma (zona pellucida), and that when the follicular epithelium is detached from the internal theca by the action of the fixative reagents, the membrana limitans externa separates into two layers, as displayed in the figures he gives (figs. 58 and 60, pl. X). "The inner of the two layers," continues the author, "is connected with the outer ends of the follicle cells, and is possibly formed by them in the same way that the external limiting membrane of the central nervous system is formed by the outer ends of the neuroglial cells. The outer layer is connected with the innermost flattened cells of the internal theca, and it reacts like other connective tissue structures to connective tissue stains." He says further "Its function is unknown, but its constant presence indicates utility, and it possibly regulates the passage of different materials in opposite directions to and from the follicle."

In regard to the staining affinities of the membrana limitans externa and the zona pellucida in human material, our own observations do not correspond with those of Robinson. In general, allowing for the difference in the density of the two structures—the membrana being exceedingly delicate as compared with the zona—the staining reaction appears to be very similar—both take up the plasma stain as distinct from the nuclear stain. The appearance of the membrana limitans externa is in every case very similar to that of the capillary walls, in fact of all vessels which possess no muscular coat.

In sections of the rabbit's ovary, which were examined after being subjected to Mallory's connective tissue stain (fixative: Flemming's (strong) formula), both the zona and the membrane were tinted blue alike. It was noticeable that in the rabbit the membrane was a somewhat denser layer than is revealed in the human Graafian follicle.

Observations on the human material at my disposal confirm the view that the cells of the stratum granulosum are very prone to separate from the inner surface of the internal theca of the follicle, and when this separation takes place, the layer which intervenes, viz. the external limiting membrane, invariably remains attached to the connective tissue elements of the internal theca. The separated layer of the stratum granulosum exhibits little appearance on its outer surface of any but the feeblest connexion with this membrane, and in most cases shews little evidence of any connecting fibres. In some instances it would appear as if the union between the stratum granulosum and the membrana limitans externa was sufficiently intimate to lead to a tearing away of a layer of this latter structure, along with the cells of the stratum granulosum, so separating it into two layers, as described by Robinson, the inner being connected with the outer surface of the cells of the stratum granulosum, the outer still remaining adherent to the inner surface of the internal

theca, though no difference in staining reaction such as is described by Robinson could be discerned. The accompanying figures (figs. 14 and 15) represent both conditions.

The fact that the ease with which the stratum granulosum appears to separate from the membrana limitans externa seems to vary with the ripening of the follicle, would suggest that this separation is a natural process, and not necessarily an artefact as frequently supposed. The fact, too, that the membrana limitans externa is at times prone to split into an external and an internal layer, where separation of the stratum granulosum takes place from the inner surface of the internal theca, inclines one to the view that possibly this intervening layer between these two mentioned structures may be in fact permeated by an irregular lymph space, which weakens the bond between the internal theca and the layer of the contained follicular cells, and so renders more easy the separation of the two structures. For apart from the evidence forthcoming in the examination of unruptured follicles, there is the circumstance that immediately after the bursting of the follicle and prior to the formation of a corpus luteum, the entire stratum granulosum is shed and disappears, leaving only the internal theca and the membrana limitans externa lining it. Moreover, through the courtesy of Professor Robinson I have been able to note the fact that in the ferret the ovum after it has escaped from the Graafian follicle is not only surrounded by the cells of the cumulus, but also has connected therewith a considerable amount of a layer corresponding to the stratum granulosum, thus proving that at the time of rupture the stratum granulosum was in part or in whole discharged. These observations seem to point to the separation of the stratum granulosum from the internal theca as a normal process, and not necessarily an artefact as so many hold it to be.

This matter will be again referred to when the mode of rupture of the follicle is discussed.

In concluding this section relating to the liquor folliculi, mention must be made of the varieties of coagulum met with in the follicle, even when subjected to the same fixing reagent. In many instances the coagulum exhibits the appearance of fine ground glass, in others the granulations are coarser. In some it takes on the form of an open meshwork. In all, as best seen at the edges, the reticulum varies much in appearance, in some it is fine, in others, coarse. These appearances, met with in what seem normal follicles, combined with the variety of tint displayed when subjected to the same staining reagent, suggest that the physical and chemical constitution of the liquor folliculi is not always constant, but is undergoing change, it may be by the addition or subtraction of constituents which affect its density or alter the character of its composition.

The Sheath of the Follicle

As usually described the specialised part of the ovarian stroma around the follicle consists of two not very clearly defined zones, the internal theca and

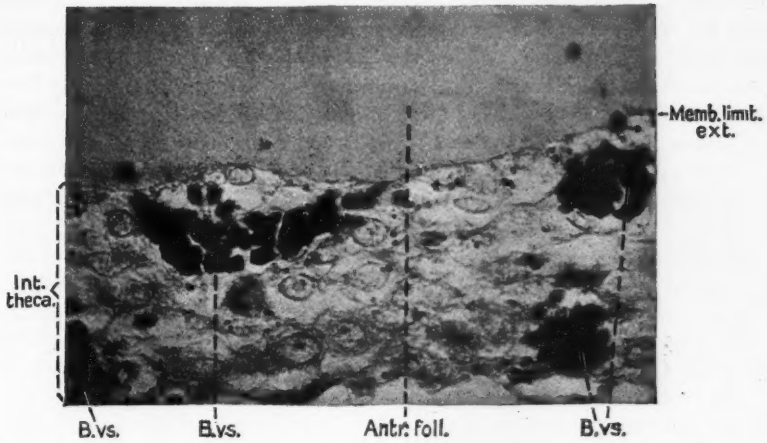

Fig. 14. Section shewing the appearance of the internal theca (*int. theca*) when the stratum granulosum has become separated from it. The membrana limitans externa (*mem. lim. ext.*) is seen adherent to the internal theca. *B.vs.* capillaries within the internal theca filled with blood corpuscles. ×700. Specimen O. 1. 103

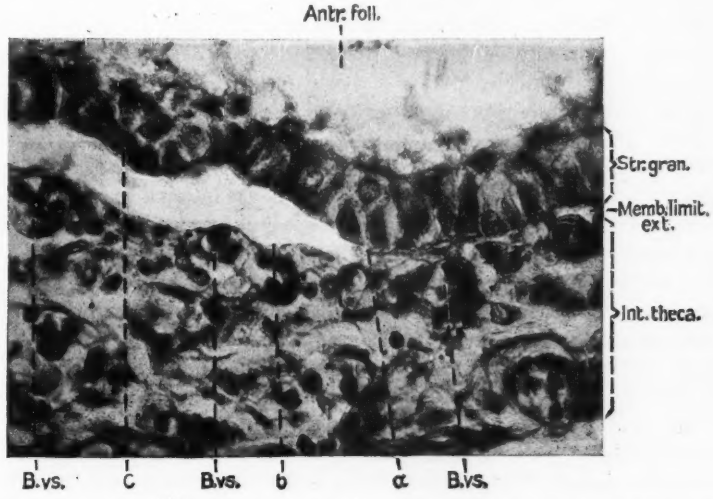

Fig. 15. Section of the wall of a follicle shewing stratum granulosum (*str. gran.*) and internal theca (*int. theca*) lying in apposition, with the external limiting membrane (*mem. lim. ext.*) in between; at the point *a* this layer is seen to split, one layer (*b*) adheres to the internal theca, the other (*c*) clings to the stratum granulosum; the interspace between is probably a lymph space. *B.vs.* capillaries of internal theca: *antr. foll.* antrum folliculi. ×600. Specimen O. I. 20. 5.

the external theca. The internal theca is composed of a loose cellular stroma made up of round and spindle-shaped cells, and has a capillary net-work throughout its substance. To the outer side of this lies the external theca, in which zone, the tissue is denser, more fibrillar, and less vascular, though here the blood vessels are larger, and furnish the branches which supply the capillary plexus of the internal theca. In the theca externa there are also described a number of hollow spaces which are interpreted as enlarged lymph channels.

A study of the appearance of the internal theca reveals the fact that this layer becomes richer in capillaries as the growth of the follicle proceeds (see Nagel, (23), p. 56); so also the round cells become larger and more numerous. In some instances I have reason to believe that the theca interna over the area which corresponds to the site of the cumulus is more vascular than in other parts of the circumference of the follicle, a fact which, as will presently appear, has some significance.

Not only does the internal theca appear to be richer in capillaries, but in several instances, one of which is here represented (fig. 16), the capillaries are not confined to the theca interna, but invade the substance of the follicular epithelium, where it forms the base of the cumulus or discus proligerus.

So far as I am aware, no mention of this condition has hitherto been made, and I was inclined to regard the first specimen I observed of this appearance as of the nature of a haemorrhage. The sections, which were stained with Mallory's connective tissue stain, revealed the blood corpuscles as tinted a brilliant scarlet, a feature which enabled us to trace with ease their disposition and arrangement. By adopting a method of reconstruction it was possible to prove the continuity of these collections of blood corpuscles, and to trace their connexion with the capillaries of the internal theca; there was also distinct evidence that around these collections of blood cells there was a delicate membrane, directly continuous with, and presenting the same appearance as, that enclosing the capillary channels of the internal theca. Obviously it was hazardous to base any conclusion regarding the nature of this condition on its occurrence in one particular specimen, consequently a search was made to see whether it occurred in other follicles. The result was confirmatory, for in several other instances the presence of blood corpuscles similarly grouped and ensheathed was clearly demonstrated, though it must be admitted, that but for the differential staining produced by the employment of Mallory's formula the occurrence of this particular arrangement might have been overlooked.

On reviewing the evidence, however, it was particularly noticeable that, with one exception, all the specimens exhibiting this feature were derived from the same source, a woman who died of heart disease, and regarding the post mortem of whom the report records the occurrence of "back pressure" changes in many of the viscera. This condition may naturally be regarded as answerable for the appearance displayed, and might be accepted as conclusive evidence that the arrangement of the capillaries represented is abnor-

mal, were it not for the fact that a similar condition was met with in the ovary of a woman aged 35 who died of laudanum poisoning, in which case the ovum contained within the follicle was degenerate. It may be that the administration of this drug is alike responsible for the unusual appearance observed. Whatever be the cause, and whether or no we are to regard the incidence of

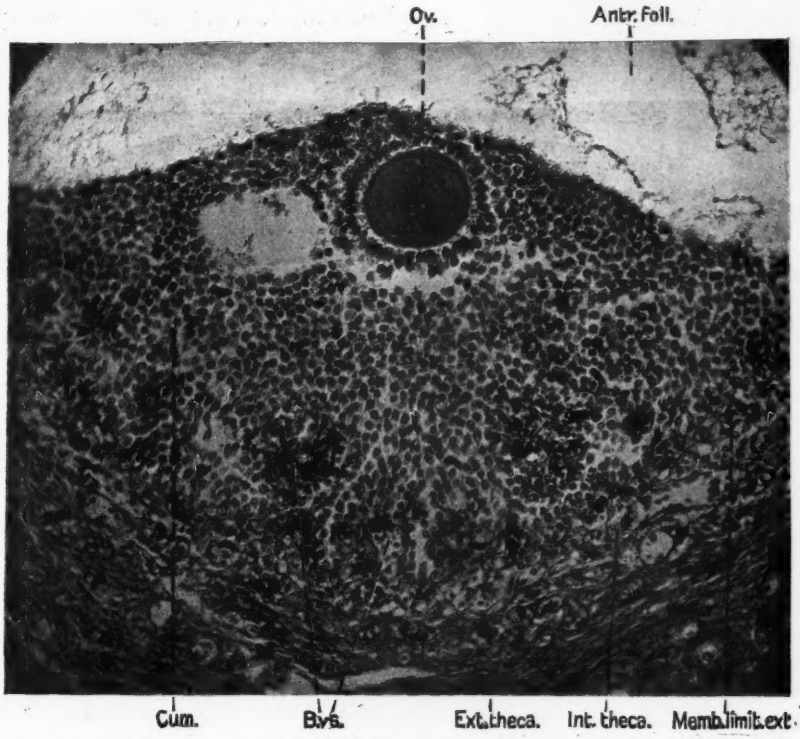

Fig. 16. Section through the cumulus of a human Graafian follicle shewing ovum *in situ* surrounded by the zona pellucida and corona radiata. The base of the cumulus is invaded by capillaries containing blood cells. These are seen to be enclosed by distinct walls similar to those displayed by the capillaries of the internal theca (*int. theca*). The membrana limitans externa (seen at *mem. lim. ext.*) seems to disappear as a definite layer in the region corresponding to the base of the cumulus (*cum.*). *Ext. theca*, external theca; *antr. foll.* antrum folliculi. × 200. Specimen 453 F. 20. 4.

this feature as normal or abnormal, its occurrence is worthy of record, since possibly, if normal, it may be the means of providing the ovum with an increased source of nutrition, whilst if abnormal, it may account for degenerative conditions which may arise in like or similar circumstances.

It is interesting to note that in the specimens taken from the woman who died of heart disease, the presence of this condition did not appear to have any

deleterious effect on the ova, for in the sections examined these appeared to be normal. In the case of the woman who died from laudanum poisoning it is open to doubt whether the degenerated ovum was a direct result of the poison or secondary to the vascular changes present.

There arises in this connexion the question of the relation of the membrana limitans externa (basal membrane) to these capillary invasions. It would appear from an examination of the specimens in which this peculiar distribution of the vessels occurs, that in the neighbourhood of their entry into the cumulus the membrana limitans externa has disappeared, and there seems no line of demarcation to separate the follicular cells from the connective tissue elements of the theca interna.

It must not be assumed that the cases I have recorded include all the instances of blood within the follicle. Not unfrequently undoubted cases of haemorrhage are met with, occurring either as scattered masses of blood corpuscles within the substance of the follicular cell work, or else discharged in bulk into the antrum folliculi. These collections we generally found associated with molecular changes in the walls of the follicle, and also combined with marked degenerative changes in the ovum itself. It may be that the appearances I have noted, and here figured, are only an early stage of the process which ultimately results in a diffuse haemorrhage. If so, they may be of interest as shewing how this destructive process leading to the atresia of the follicle is induced.

Of the changes which take place in the structure of the internal theca at the point corresponding to the site of its ultimate rupture little need be said. As the covering wall of the follicle in this region becomes thinner its vascularity becomes reduced.

Already reference has been made to the membrana limitans externa (basal membrane). This, as has been said, intervenes between the inner surface of the theca interna and the peripheral cells of the follicular epithelium which lie within the follicle. It is shown *in situ* in fig. 17.

As already described, when separation occurs between these two constituents of the follicle, the bulk of the membrana limitans externa (basal membrane) remains adherent to the flattened cells forming the inner surface of the internal theca (see fig. 14). For this reason, the term "basal membrane" as applied to it, suggesting its intimate connexion with the cubical cells of the stratum granulosum which overlie it, is misleading. Its behaviour and anatomical disposition are more in accord with the interpretation of the term "external limiting membrane" applied to it.

It should be noted that in many parts of the section of the wall of the follicle this limiting membrane is the only layer which intervenes between the capillary stream and the contents of the follicle, and if so be, as has been suggested by its tendency to split into two layers, this limiting membrane contains a series of lymph channels within its substance, it may well be that it forms a structure of no little importance, not only in regard to the nutrition

of the follicular contents, but also in connexion with the process involving the rupture of the follicle itself.

The external theca. As already explained, there is no clear line of differentiation between this and the internal theca; it differs from the latter in the absence of a capillary network, and the greater density of its constituent layers, which are largely composed of fibrillar tissue, derived from the surrounding ovarian stroma, and concentrically arranged around the Graafian follicle. It is to the nature of this tissue that attention must first be directed.

Schäfer (29), p. 643) thus describes the ovary: "Each ovary is formed of a solid mass of fibrous-looking tissue (stroma), which contains between its fibres

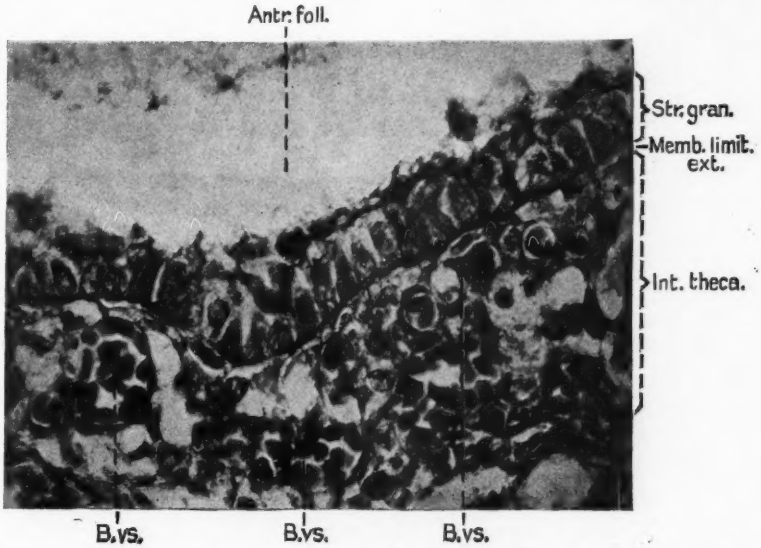

Fig. 17. Section through the wall of a human Graafian follicle shewing stratum granulosum (*str. gran.*), membrana limitans externa (*mem. lim. ext.*) and internal theca (*int. theca*) all in contact. *B.vs.* capillaries of internal theca containing blood. *Antr. foll.* antrum folliculi. ×700. Specimen 453 B. 27. 3.

very many elongated cells like those of embryonic fibrous tissue...Along the line of attachment (hilum) blood vessels and nerves enter and leave the ovary, and accompanying these is a strand of fibrous tissue which contains plain muscle amongst its fibres."

Piersol (24), p. 1987) says of the cortex of the ovary: "The stroma cells somewhat resemble the elements of involuntary muscular fibre in appearance," and in reference to the medulla says it consists of fibro-elastic tissue and smooth muscle accompanying the larger vessels. In this connexion it may here be stated that in a specimen stained with Weigert's elastic tissue stain the only situation in which elastic fibres were recognised was in relation to the walls

of the vessels—neither in the general stroma of the organ nor in the follicular walls was there any evidence of the presence of elastic tissues.

Nagel ((23), p. 49) states that in the zona vasculosa there is "an extension from the muscular tissue of the broad ligament along the larger vessels, better marked in mammals than in man."

It would seem, therefore, that in the groundwork of the ovary we have to deal with fibrous and muscular elements, the differentiation of which is not always an easy matter.

Winiwarter ((35) and (36)) states that the distribution of the muscular element in the human ovary is identical with that exhibited in the cat, in which

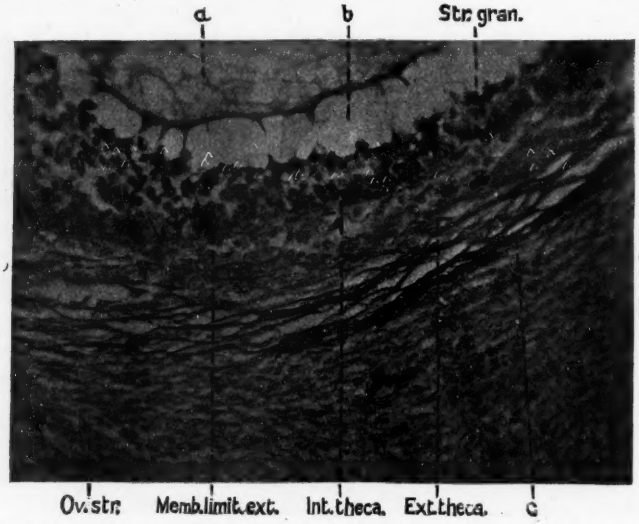

Fig. 18. Section through the wall of a human Graafian follicle. *a*, coagulum within antrum folliculi; *b*, retraction space between coagulum and stratum granulosum (*str. gran.*); *int. theca*, internal theca with capillaries; *ext. theca*, external theca with (*c*) bundles of smooth muscular fibre differentially stained with safranin and light green. ×400. Specimen O 2. 52. 3.

animal he describes it as entering into the formation of the external theca of the Graafian follicle. Before I was acquainted with his conclusions I was myself engaged in analysing the nature of the fibres of the external theca, and had been led independently, through the staining reactions, to suppose that all the fibrils were not of a like nature.

My attention was first directed to this whilst examining some specimens stained with safranin and light green. With this reagent some of the concentric fibres of the external theca were stained a pronounced pink, which stood out in contrast to the grayish green tint of the surrounding stroma. Fig. 18 exhibits the appearance in a section through the follicular wall.

The coagulum within the antrum folliculi is stained a bright green in the

original specimen, the membrana granulosa is purplish in tint. The theca interna is coloured a purplish gray, whilst in the theca externa there are elongated fibres which, staining a pronounced pink, stand out in marked contrast to the surrounding grayish green stroma. Confirmatory evidence was

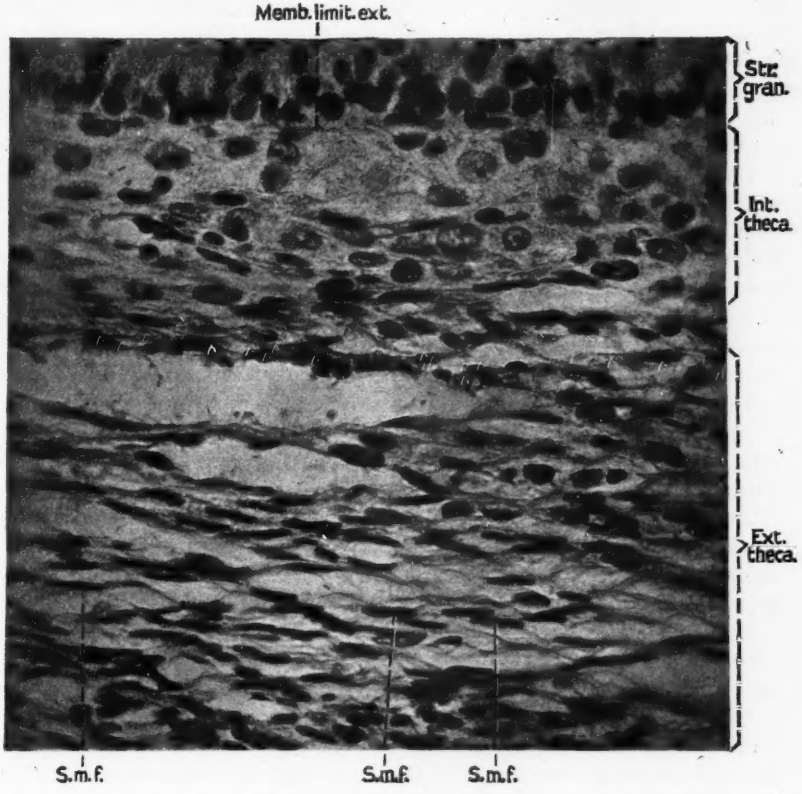

Fig. 19. Higher magnification of a portion of the same follicular wall as that shewn in fig. 18. *Str. gran.* stratum granulosum; *int. theca*, internal theca; *ext. theca*, external theca, in which are seen the fibres, *s.m.f.*, which have been identified as smooth muscle fibres. *Mem. lim. ext.* membrana limitans externa, in this specimen not very clearly defined. × 600. Specimen O 2. 80.

also obtained from other specimens stained by Mallory's method, wherein corresponding groups of fibres were stained distinctly purple in contrast with the surrounding bright blue colour; whilst in other sections of different follicles subjected to the influence of Congo red, the same tissue elements were revealed stained a dull violet, contrasted with the grayer colour of the tissue around. It is only fair to say that these results were not obtained in all the specimens examined, but so convinced was I of their significance that I em-

ployed other and more refined methods, with confirmatory results. Fearing lest my observations might be biassed, I handed over some unstained sections to my friend Mr H. M. Carleton, the Demonstrator in Histology, with the request that he would subject them to a careful examination. This he took great pains to do, and finally admitted that on histological grounds, no less than by reason of the staining reaction, the tissue undoubtedly contained smooth muscle fibre. From my own material I am enabled to furnish a figure of a highly magnified microphotograph which demonstrates these features (fig. 19).

Whilst there is thus undoubted evidence of the presence of smooth muscle in the external theca of the follicle, it is interesting to note that with certain reagents, we may obtain, under a low power, a general view of the distribution of this muscular element throughout the substance of the ovary as seen in section. This is best demonstrated in sections stained with safranin and light green; the colour differentiation effected is such as to indicate the presence of a tissue of a peculiar staining quality which invades the substance of the ovary along the line of the great vessels and follows them outwards as they reach the area of their distribution towards the cortex. The general arrangement of this particularly coloured zone conforms closely to the distribution of the blood vessels as indicated in the figure which Clark (6) has published in his account of the blood vessels of the ovary. As may there be seen, the smaller vessels are traced to the walls of the follicle, accompanied no doubt by the strands of smooth muscle, whose general course is indicated by their greater affinity for one of the constituents of the double stain. In the specimen examined the contrast between the differently stained areas was sufficiently pronounced to indicate the general distribution of the smooth muscle.

In the human ovary it thus appears that smooth muscle is present in considerable quantity, not so abundant as may be seen in lower forms, but still in such amount as to play a considerable part in the functioning of the organ.

According to Winiwarter ((36), p. 639), all attempts have hitherto failed to demonstrate the presence of this muscular element by experimental means. I therefore consulted my friend Dr Gunn, the Professor of Pharmacology here, who, after having had his interest enlisted in the question, determined to make a fresh attempt. He reports as follows: "The ovary (a rabbit's) was suspended in a bath of oxygenated Locke's solution at body temperature. Movements were recorded by a light-lever of high magnification, the method used being the same as has been widely employed for the isolated uterus and other organs. No spontaneous movements were shewn by the ovary. In one experiment the ovary of a full-grown virgin rabbit shewed on the addition of adrenaline to the Locke's solution (in concentration of 1 in 200,000) a contraction of the ovary characteristic of smooth muscle. Adrenaline stimulates the sympathetic nerve ends in smooth muscle. The sympathetic nerve is a motor nerve to the rabbit's uterus. The experiment therefore indicated that the ovary contains smooth muscle, innervated by the sympathetic, and that the innervation of

the ovary is qualitatively the same as of the uterus (in the rabbit). With high lever magnification the amplitude of excursion was very small, indicating a very small amount of contractile tissue."

This experiment seems to set at rest all doubts as to the presence of functionally active muscular fibres within the stroma of the ovary, and as we have already seen that fibres answering to the histological details of smooth muscular fibres and reacting similarly to selective stains occur within the wall around the Graafian follicle, it is evident that we have to hand a means which may play a not unimportant part in the rupture of the follicle.

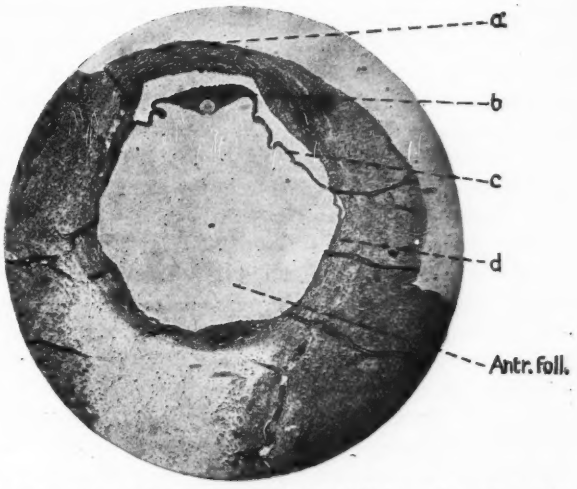

Fig. 20. Section through a nearly ripe human Graafian follicle; *a*, the surface of the ovary; here the follicular wall is only about ·2 mm. thick; *b*, the cumulus containing the mature ovum, note that it lies on the superficial aspect of the follicle, immediately opposite and close to the thinnest part of the follicular wall. Both the cumulus (*b*) and the stratum granulosum (*c*) are separated from the internal theca in the upper hemisphere; *d*, the external and internal thecae combined, the magnification is not sufficiently high to differentiate these layers. In the lower hemisphere of the follicle the cells composing the stratum granulosum are still adherent to the inner surface of the follicular wall, the membrana limitans externa alone intervening; the magnification is not sufficient to shew this layer; *antr. foll.* antrum folliculi. ×18. Specimen 453 A. 35. 4.

The Rupture of the Follicle

Having passed in review the various structures which enter into the formation of the Graafian follicle and its contents, it may now be possible to discuss the means by which the follicle ultimately ruptures and sheds its contents. Before, however, proceeding to consider this question, it may not be without advantage to reproduce a microphotograph of a Graafian follicle which must have nearly reached the stage at which its rupture was imminent, to judge by the appearances displayed (fig. 20).

The estimated size of the follicle is 2·00 × 1·96 × 1·63 mm. As is readily seen, the superficial wall of the follicle, i.e. that separating its cavity from the surface of the ovary, is thin, only 0·2 mm. thick. The ovum contained within the follicle is judged to be mature, since there is present in it a divided first polar body, together with a second polar body, whilst the nucleus appears to have returned to the resting condition. A figure of this oöcyte has already been published in my previous paper on the maturation of the ovum (33). For all these reasons, we are justified in supposing that the follicle is ripe, and has reached the stage in its existence when its collapse, and the liberation of its contents, cannot for long be delayed if the physiological necessity arises.

But an examination of the figure enables us to realise certain unusual features. First, we recognise that the ovum, surrounded by the cumulus, is so disposed that it lies superficially within the follicle, and near, and in immediate correspondence with the line of the stigma—the site corresponding to the point of rupture. But secondly, it is obvious that throughout the superficial hemisphere (i.e. that directed to the surface of the ovary) the stratum granulosum with the cumulus has become detached from the inner surface of the internal theca; elsewhere, over the inner surface of the posterior hemisphere, it still remains attached.

Obviously no better arrangement could be devised for the expulsion of the ovum than that shewn here, for if the rupture be due to an increase in internal pressure, the ovum would naturally, by the bursting pressure, be forced through the orifice made in the weakened wall when that gave way. Unfortunately, as we have already seen, the position of the ovum and the cumulus is not always superficial, but may be, and often is, situated in relation to the deep surface of the follicle, at a point opposite and farthest removed from the stigma, in which case it is difficult to understand how, when the rupture occurs, the discharge of the ovum is effected. Under these circumstances the doubt arises in one's mind, as to whether the ovum is not more likely to remain lodged in the bottom of the empty cup.

The detachment of the cells of the stratum granulosum from the inner surface of the internal theca is a matter which has already attracted a considerable amount of attention. The prevailing opinion is that the condition is to be regarded as an artefact—that it is due to the retraction induced by the coagulation of the liquor folliculi. Such an explanation seems feasible, and is possibly the one that comes readiest to hand; before accepting it, however, there are some other considerations that must be taken into account.

In the numerous examples of this condition which I have studied, I have been struck with the fact that there is not always such a correspondence in the contours and area of the retracted surfaces of the stratum granulosum and the internal theca as one might expect if the separation of the layers were effected by such mechanical means. It is not uncommon to find the stratum granulosum floated well into the centre of the follicle, and twisted and infolded in such a way as to suggest that these layers were afloat in the fluid

contained within the follicle at a time prior to its coagulation. Further, they often exhibit appearances as if undergoing disintegration, and are frequently fragmented. In dealing with human material it is only fair to say that putrefactive processes must not be overlooked. Yet withal, I confess I am by no means assured that the condition is thus easily explained as being due to the effects of coagulation by fixation.

There are additional reasons for hesitating to accept this view. First, the case in which the cumulus is so disposed as to lie on the deep surface of the interior of the follicle, the site assigned to it by Nagel and others as normal. Under those circumstances it is difficult to see, as has just been observed, how by any pressure sufficient to burst the follicle the ovum could be expelled through an opening opposite in direction to the force to which it was being subjected. As has been said, a more reasonable supposition would be that it would be left in the bottom of the cup, and this, be it observed, is what is supposed to have happened in those cases of ovarian pregnancy which have been recorded, the explanation offered being that the ovum has failed to escape from the ruptured follicle and that the entering spermatozoön has fertilised it *in situ*.

Second. Thanks to the kindness of Professor Robinson, I have had an opportunity of seeing, amongst his collection of ferret material, an ovum, just within the oviduct, apparently recently discharged from its follicle, which, besides being surrounded by the cells of the cumulus, had, attached to these, tags of tissue which could only be accounted for on the supposition that they were remains of the sheet of the surrounding stratum granulosum.

Third. In one case I had the opportunity of examining a human Graafian follicle which must have been quite recently ruptured. In this I failed to find any trace of follicular cells—all that remained was the enfolded and engorged internal theca, very definitely lined internally by the membrana limitans externa, without any trace, so far as I could see, of any follicular cells overlying it. Within what was left of the cavity of the follicle were a few scattered blood cells only[1].

This raises of course the vexed question of the origin of the corpus luteum. Von Baer in 1827 propounded the view that the corpus luteum was derived from the theca interna. This conception has been supported by Valentine, His, Rokitansky, Kölliker, Gegenbaur, Paladino, Nagel, Bonnet, Schottländer, Minot, Williams, Clark and others.

On the other hand Bischoff in 1842 expressed the opinion that the corpus luteum is derived from the follicular epithelium. This view has received support from Meckel, Pflüger, Luschka, Waldeyer, Sobotta, Honoré, Marshall, Van der Stricht, Heape, and Kries, amongst others.

Rabl in 1898 suggested a compromise, and concluded that the lutein cells

[1] It is interesting to note that this specimen was obtained from the ovary of a woman whose uterus exhibited evidence of the onset of menstruation.

have a double origin, arising both from the membrana granulosa and from the theca interna[1].

Into this controversy I am not at present prepared to enter; all I can say is that the human specimen I have here mentioned appears to confirm in every respect the original contention of Von Baer.

There can be little doubt but that the liquor folliculi serves two useful purposes: it acts as a source of nutrition for the ovum, as well as providing a means for its protection. The production of this fluid by the disintegration of the follicular cells through the agency of the so-called bodies of Call and Exner has been already discussed (see p. 14), and need not now be further alluded to. During this process of the dissipation of the follicular cells, with a concomitant increase in the size of the antrum folliculi, there also appears to be taking place a reproduction of these follicular cells to replace the wastage, as evidenced by the occurrence of mitotic division observed amongst them. To what extent this takes place it is difficult to say, but apparently there comes a time when this source of reinforcement is reduced to the thin single layer of cubical cells which represents all that is left of the stratum granulosum. In some instances, the conditions are such that this remaining layer may all but disappear, in fact in some cases I have failed to find evidence of it in parts of the circumference of the follicle.

Support is given to this view by the observations of Miss Lane-Claypon (16, p. 42) on the ripe Graafian follicle of the rabbit, in which she describes "almost complete disintegration of the membrana granulosa."

A fact of some interest, be it noted, is that this condition is not necessarily met with in follicles which one would regard as fast approaching their rupture, as judged by their very superficial position and the thinness of their overlying wall. This activity on the part of the follicular cells is no doubt sustained by the nutrition derived from the fluids of the blood through the agency of the capillaries of the internal theca, and possibly the liquor folliculi itself may be increased in bulk by an admixture of constituents derived from both sources.

In this connexion, it is well to remember that interposed between the peripherally placed follicular cells and the capillary zone of the internal theca, there is the membrane which has been already alluded to as the membrana limitans externa (basal membrane). Now, as stated, there is considerable doubt as to the constitution of this membrane. We have seen that the union between this membrane and the follicular cells is generally speaking very feeble, and that the follicular cells are extremely liable to be detached therefrom, it may be by artificial means, or possibly as the result of a normal process. In the accompanying figure (fig. 21) there seems strong evidence for believing that the separation of the stratum granulosum and the internal theca is effected by the infusion of fluid between the two layers of the membrana externa, and not by the dragging away by retraction of the membrana externa from

[1] For the literature of this subject I am indebted to the papers of J. G. Clark (6) and F. H. Marshall (19).

the internal theca, else how can we account for the appearance of distensions within these spaces and the concavity of their walls?

As a consequence of this separation, whilst in the majority of cases the bulk of the membrana limitans externa adheres to the inner surface of the internal theca, yet the evidence produced (see fig. 15) of the splitting of this layer so that one lamina adheres to the follicular cells, whilst the other remains in contact with the internal theca, suggests that the structure of this layer is not so homogeneous as is usually described, but that sandwiched between its

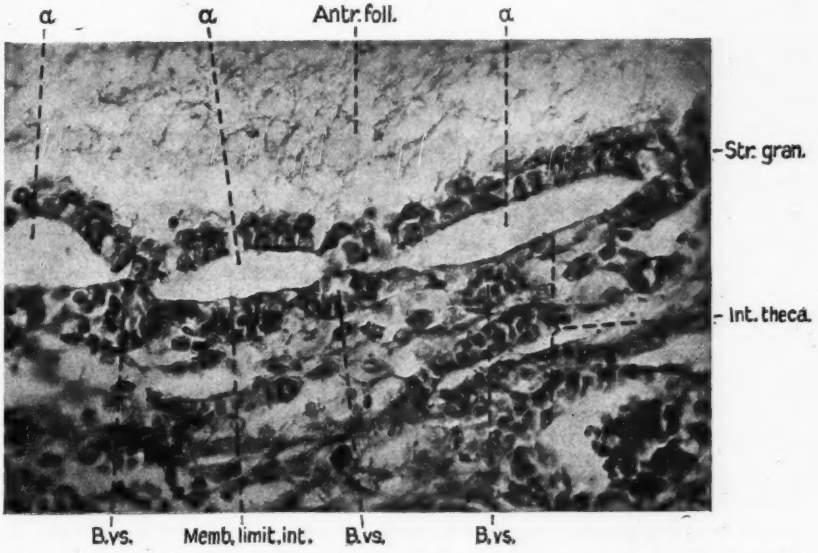

Fig. 21. Section of human follicular wall shewing the commencement of the separation of the stratum granulosum (*str. gran.*) from the internal theca (*int. theca*). This appears to involve the splitting of the membrana limitans externa through the distension of the lymph spaces in it, so that larger spaces (*a, a, a*) are produced, the walls of which through their concave contours afford evidence of a pressure from within, due to the accumulation of fluid inside the spaces. Note the position of the capillaries (*B.vs.*) of the internal theca (*int. theca*) in relation to these spaces (*a, a, a*) the walls of which are formed by the split membrana limitans externa, one layer of which adheres to the internal theca, the other forming what looks like a basement membrane to the external layer of cells of the stratum granulosum. *Antr. foll.* antrum folliculi filled with a reticulated coagulum. ×400. Specimen 453 B. 30. 6.

inner and outer strata there may be a weaker element, or, what is more probable, a series of lymph spaces in direct contact with the capillaries of the internal theca, as seen in the figure, on the one hand, and the bedded bases of the follicular cells on the other.

This splitting of the external limiting membrane is a feature to which Robinson ((27), p. 320, plate X, figs. 58 and 67) has already called attention, though he attributes it to the use of fixatives. Granted that it is so, it may be

the means of revealing potential spaces which at the time may not be distended, but this in no wise precludes the possibility of these being tissue fluid channels.

My reason for dwelling on these facts is that they may possibly afford an explanation of what happens when the follicle bursts. Various opinions have been expressed in regard to the mechanism which brings about this phenomenon. The generally accepted view is that by a gradual increase in the bulk of the contents of the follicle such a pressure is induced as will lead to the rupture of the gradually weakening wall in the region of the stigma.

On the other hand, some, in order to bring the details more into accord with the accepted facts, suggest that the rupture of the follicle is induced by a sudden increase in the follicular pressure.

Nagel ((23), p. 60) and his followers attribute the rupture to changes taking place in the tunica interna, whereby its vessels become highly developed, and its cells multiply enormously, every cell increasing in size by the growth of its protoplasm, at the same time the protoplasm becomes filled with a peculiar crumbling mass of which nothing more definite is known, from which the whole inner wall of the follicle (in the fresh condition even before its rupture) acquires a yellowish colour. The tunica interna thus altered has an undulating appearance, while its cells, which are now called lutein cells, and form a strong layer many rows thick, are arranged in the form of papillae, into every papilla runs a much-branched vessel. Through this growth of the lutein cells the contents of the follicle are pushed towards the thinnest part of the follicle (stigma) on the surface of the ovary, and thus the follicle is brought to its rupture.

In respect of this I can only say that my own observations have not enabled me to recognise these conditions in the still unruptured, though apparently ripe follicle. The appearances described are such as are readily recognised in the freshly ruptured follicle, preliminary to the formation of a corpus luteum, though here unfortunately we are unable to form other than an approximate estimate of the time which may have elapsed between the rupture and the examination of the specimen.

Clark (6), in discussing the matter, in part attributes the dehiscence of the follicle to the peculiar arrangement of the vessels of the ovary, and was able to demonstrate the rupture of the follicle following the introduction of a carmine-gelatine injection. He also considers the occurrence of haemorrhage within the follicle more frequent than its absence.

Heape (13) considers that in the rabbit the rupture is induced by the stimulation of the erectile tissue, and not simply as a result of internal pressure arising from increased vascularity, or a greater amount of liquor folliculi.

In a series of experiments Schochet ((30), p. 241) indicates that the liquor folliculi possesses a digestive enzyme that can be demonstrated by dialysis and other tests. As a tentative interpretation it is suggested that the rupture of a Graafian follicle is due in part to the digestion of the theca by the liquor folliculi.

Winiwarter ((36), pp. 640–41), in discussing the function of the smooth muscle met with in the ovary, reviews the suggestions previously made by Rouget (28), and Aeby (1), that the muscular tissue plays its part "by setting in action a complex mechanism subject to physiological conditions of which we are ignorant, and which simple galvanic stimulation cannot reproduce," the conclusion being that "the ovary, together with all the internal genital tract, can undergo erection under the influence of a stimulus aroused, in the ovary, by the distension of the Graafian follicles; the increase of tension in the ovarian stroma brings on the rupture of the follicle, after which relaxation follows; it is therefore the muscular tissue of the mesovarium which plays the active part." This hypothesis is also supported by Grohe (11).

Winiwarter's own conclusion is that the muscular tissue in the mesovarium acts in part by controlling the venous return from the organ, thereby conferring on it an erectile power, probably associated with the period of rut, or, it may be, aroused by the stimulus of coitus, whilst he suggests that the presence of smooth muscle in the external theca of the Graafian follicle may be a determining cause of its rupture.

Furthermore, it has frequently been suggested that the congestions which occur within the pelvic organs at the menstrual periods, and the turgescence of the associated organs which may occur during coitus, may have something to do with the rupture of the follicles.

It is too complex a problem here to discuss the question of the relation of ovulation to menstruation, suffice it to say that the bulk of the evidence seems to point to the fact that there is an intimate association between the two phenomena, and that consequently those vascular changes which we associate with the one may be in part responsible for certain of the processes connected with the other.

As Eden puts it ((7), p. 6): "It is undoubtedly true that ovulation and menstruation are closely related to one another. Whether they are coincident or consecutive, and if consecutive, which precedes the other, we do not know with certainty."

Barnes ((2), p. 455), Dr Clelia Mosher (21) and Helen MacMurchy ((17), p. 909) quoting Giles ((10), p. 115) and Dr Mary Jacobi (15), are all agreed that there is normally a rise in blood pressure for a day or two prior to menstruation, and a fall immediately on the onset of the flow.

I am aware that the occurrence of apparently ripe Graafian follicles has been recorded in young children prior to menstruation, and even in some instances in the new-born child (Nagel (22), p. 413), but there is no evidence that these ever ruptured or that the ova therein contained were capable of fertilisation; it is much more probable that the follicles became atretic.

Considering the foregoing suggestions and the observations on which they are based, it would appear that well-nigh everything that could be said on the subject had been already stated. A little reflection, however will, I hope, induce the reader to believe that there are other ways of interpreting the

phenomena, and so bringing them more in line with what experience would support.

I have endeavoured to suggest that the main function of the liquor folliculi is to nourish, conserve, and protect the delicate ovum as it lies within the follicle. Evidently a time arrives when, from the appearance presented, the further production of the liquor folliculi by the disintegration of the follicular cells is arrested, as evidenced by the reduction in number and change in character of the residual follicular cells. At this stage we may assume that the pressure within the follicle is stabilised, and may remain for unknown periods undisturbed. It is therefore hard to believe that the pressure within the follicle can be rapidly raised by any sudden increase in the amount of the fluid derived from the follicular cells.

We have around the follicular cyst, if such I may call the liquor folliculi enveloped by the stratum granulosum, a capillary plexus subject to all the controlling influences of the sympathetic nervous system.

We have already alluded to this capillary zone as essential to the nutrition of the follicular epithelium, though to what extent the liquid constituents of the blood may contribute to the fluid bulk of the liquor folliculi we have no information; but assuming that the liquor folliculi is in main the product of the follicular cells, it by no means follows that, since the source of that supply is no longer active, the fluid derived from the blood in the capillaries contributes no further to the increase in fluid contents of the follicular cyst; controlled as is this supply by the sympathetic, it must necessarily react to such stimuli as induce changes in the circulation directly concerned, or, it may be, in harmony with vascular changes induced in the tissue around.

Sexual thoughts, sexual desires, coitus, the congestion associated with menstruation, may all play a part, with what result?—the immediate and sudden increase in pressure, involving, it may be, the transudation of a greater quantity of the fluids of the blood, and thus increasing the pressure contents of the follicle to its straining point. I suggest that in this process, when dealing with a follicle the contents of which are ripe for discharge but quiescent, the effusion of fluid poured out from the capillaries invades those lymph channels which, we have reason to believe, intervene between the cells of the stratum granulosum and the internal theca, thereby tending to separate the granular layer from the inner wall of the follicle, and thus leading to the release of the cumulus and its anchoring layers, so that it, with the contained ovum, lies free and floating within the cavity of the follicle in such a way that it must follow the stream of the fluid on its expulsion and release through the rupture.

In this way, possibly, is effected the liberation of the ovum and its associated follicular cells from the wall of the follicle, which Böhm and Davidoff (3) have suggested as an initial stage in the escape of the ovum from the ruptured follicle. According to these authors the ovum and the cells of the surrounding cumulus, or discus proligerus, ultimately come to lie free and floating within the liquor folliculi, a process which in their opinion is effected by the softening

of the cells of the pedicle of the cumulus, which thus leads to the separation of the cumulus and the contained ovum from the stratum granulosum. I do not deny the possibility of this happening, but I have not so seen it in any of the specimens I have examined, for in all the cases in which I have been able to follow, through a number of serial sections, the relations of an apparently free cumulus as displayed in some sections, on careful search I have been able invariably to trace its connexion with the stratum granulosum in other sections. For these reasons I suggest that the same end is accomplished by the stripping off of the entire follicular cyst from the inner wall of the internal theca by the rapid effusion of fluid derived from the capillaries, for in no other way can we account for the somewhat sudden increase in pressure which appears to be a necessary accompaniment of the process of ovulation.

Whilst admitting that this is a phenomenon which is dependent on effects primarily induced by the nervous mechanism controlling the circulation, we must not overlook the fact that there are other contributory causes that may play a part. We have hitherto assumed that the increase in internal pressure, effected as suggested, is the determining cause of the rupture of the follicle, for as soon as that pressure exceeds the resistance of the weakened wall of the follicle in the region of the macula or stigma, rupture must inevitably take place. On the other hand no regard has been paid to the possible influence of muscular contraction as the determining cause of the rupture of the follicle. The occurrence of smooth muscle fibre within the stroma of the ovary and mesovarium is generally admitted. Why is it there? Of what use may it be? Winiwarter ((35), p. 640) has already suggested that, by its contraction, the return of the flow of blood through the veins may be retarded, thus leading to a state of engorgement or erection of the organ, which will of course react on the capillary circulation and thus promote a more vigorous transfusion of the fluid constituents of the blood, thereby increasing the amount of lymph at certain selected and appropriate points; in this way, doubtless, assisting in increasing the bulk of the follicular contents. At the same time that author foreshadows the possibility of this smooth muscle acting as a potent factor in the rupture of the follicle, for he describes the disposition of this muscular tissue as not merely scattered throughout the stroma of the ovary, but also forming a definite layer in the external theca of the follicle.

After the demonstration which I have here given of the occurrence of a definite muscular layer in the wall of the human Graafian follicle (see figs. 18 and 19), it would seem that we are justified in assuming that this definite concentric layer fulfils some useful purpose. Its arrangement and disposition inevitably suggest that by its contraction a compressing effect, rapid and immediate, will be exercised on the contents of the follicle, thereby increasing the internal pressure and consequently determining the rupture of the follicle.

How are these facts in accord with the results of experience? Assuming that in the human female in the virgin condition there is a periodicity in ovulation coincident with that of menstruation, we have an explanation of

this apparent association, because, at that period, we have reason to believe that the ovary shares in the general engorgement which occurs throughout the genital tract; under these circumstances the conditions are such as to lead to a slow and gradual increase in the amount of the fluid contents of the follicle as derived from the blood, and distinct from those which are the product of the follicular cells, which, be it noted, in a follicle fast approaching maturity, have no further reserve to call upon. The further increase in the fluid contents of the follicle is therefore dependent on conditions determined by the local circulation, and if this condition be steadily maintained, there is little difficulty in realising how the pressure may ultimately overcome the resistance, and so the rupture of the follicle may be effected without any necessary sexual disturbance other than that involved in the psychic and emotional changes induced by menstruation.

On the other hand, there is reason to believe that ovulation takes place at other times, and in other ways, than what may be termed the routine method. It is a matter beyond dispute that under the influence of intense sexual excitement, in coitu, women are occasionally cognisant of strange happenings, which they fail to describe, but by which they are deeply impressed. Is it unreasonable to suggest that these sudden, ill-defined and deep-seated sensations are the result of the rupture of a Graafian follicle? The facts seem to fit the case. Granted the presence of an all but ripe and superficially disposed Graafian follicle in what we may term a quiescent condition; if the action of the mechanism above suggested be accepted, we have all the means necessary to bring about rapid rupture. The exalted state of the circulation will assist in the rapid accumulation of fluid within the follicle, and its subsequent distension, whilst the instant response of the muscular element in the wall of the follicle to the call of the sympathetic will immediately result in a combination sufficiently effective to ensure the rupture of the follicle and the discharge of the ovum.

If, under these conditions, this explanation be accepted, it would seem to indicate that possibly the same may occur associated with minor degrees of sexual excitement, so that, whilst in the human female ovulation may, in the ordinary way, coincide with and be associated with the vascular changes concomitant with menstruation, yet there may be no bar to the rupture of a Graafian follicle at any other time, provided such be ripe, in the sense that the ovum is mature, that the follicular cells have discharged their function by providing the necessary nutriment and affording the requisite protection, and assuming always that the follicle has acquired such a superficial position in the ovary as will permit of its rupture. There is reason to suspect that it may remain quiescent in this position until such conditions arise as may lead to increased vascular activity, or it may be the incidence of such stimuli as may react on the smooth muscle involved and so accelerate the process.

If it be doubted that the involuntary muscular fibre in the wall of the follicle can act in this way, I would urge that we have abundant evidence

of its power of contraction in the appearance displayed in the wall of the follicle after rupture, for there seems little doubt that the infolded appearance of the engorged internal theca is in major part due to the compression exercised by this contracting element, for there is no evidence of the presence of elastic tissue to bring about this result.

RÉSUMÉ

Briefly summarised the conclusions arrived at are as follows:

1. There is reason to believe that the size of the ripe human Graafian follicle is usually very much overstated in the text-books. In the author's experience it is doubtful if Graafian follicles over 5 mm. in diameter are normal.

2. The position of the cumulus is *not*, as frequently stated, always situated in the deeper part of the follicle, i.e. that furthest from the surface of the ovary. It may occur in any position, but in the material available appears to occupy a superficial position in about 50 per cent. of cases.

3. The so-called bodies of Call and Exner are follicular cells or groups of cells undergoing such changes as result in their ultimate liquefaction and disappearance to form the liquor folliculi.

4. The radial arrangement of the follicular cells around these bodies is a purely mechanical result and is in no wise concerned with the elaboration of the material which they surround.

5. The resulting liquor folliculi, primarily derived, as explained, from the follicular cells, is destined for the nutrition, conservation and protection of the ovum. It is doubtful whether it plays any active part in the subsequent rupture of the follicle, the necessary increase in the tension of the follicle being provided at the appropriate time by transudation of fluid from the blood circulating in the internal theca of the follicle.

6. The stratum granulosum may be reduced to a single layer of cubical cells. In some instances there is reason to believe that even this layer disappears.

7. In consequence of this reduction in the number of follicular cells, there comes a time when no further liquor folliculi of follicular origin is produced. When this stage is reached, there is reason to believe that the follicle may remain quiescent till other influences are brought into operation to determine its rupture.

8. The cells of the stratum granulosum rest upon the membrana limitans externa, a delicate layer which separates these cells from the inner surface of the theca interna.

9. It is noteworthy that the cells of the stratum granulosum strip off very readily from the membrana limitans externa. There is reason for suspecting that this under certain conditions is a normal process resulting in the liberation of the ovum so that it floats free in the liquor folliculi.

10. There is evidence for believing that the membrana limitans externa is not a simple single layer, but is permeated by potential lymph spaces, which on being distended lead to its splitting into two layers.

11. On this assumption the cells of the stratum granulosum are therefore separated from the capillaries of the internal theca by a network of lymph channels into which the fluids of the blood may under certain conditions be speedily discharged.

12. The rapid exudation of fluid in this situation has two consequences: it strips the cells of the stratum granulosum off the inner wall of the follicle and thus liberates the ovum and cumulus, and at the same time rapidly increases the pressure within the follicle.

13. It is noteworthy that the vascularity of the internal theca increases as the age of the follicle advances, that it tends to be more pronounced in that part of the internal theca corresponding to the site of the cumulus, and in the later stages least in the position overlying the stigma.

14. The amount of blood circulating in this capillary plexus will be determined by the conditions which control the surrounding circulation, either by increasing the flow, or, it may be, by retarding the venous return, the latter, as suggested by Winiwarter, being possibly due to the action of the smooth muscle constricting the veins and so leading to a turgescence of the tissue.

15. Such vascular conditions may be associated with the congestion and increased arterial pressure which precedes the appearance of the menstrual flux, or may be the direct result of some excitatory stimulus of a sexual kind operating through the sympathetic.

16. In either case the immediate result may be increased transudation of tissue fluid into the follicle with the results stated in paragraph 2.

17. It is probable that under what we may regard as the normal condition of ovulation in the sexually inactive female, the vascular disturbance associated with menstruation is alone sufficient to raise the intrafollicular pressure to the bursting point.

18. In the sexually active female there is reason to suppose that the same effect may be independently induced by stimuli which react through the sympathetic nervous system, provided there is at the time a quiescent ripe follicle present in the ovary.

19. In such cases no doubt the muscular element in the ovary plays an important part, more particularly that part of it which occurs in the external theca of the follicle, for this, by contracting on a follicle already undergoing distension owing to the exalted condition of the vascular supply, will naturally tend to increase the intrafollicular pressure and so lead to the rupture of the follicle.

20. If these conclusions be true it would follow that ovulation is not necessarily limited to one particular period, but that under the influence of appropriate stimuli it may occasionally occur at other times as well.

In conclusion, I must express my thanks to my Laboratory Assistant, Mr W. Chesterman, and to Miss Beatrice Blackwood, for the assistance which has enabled me to carry out this research; they have both been untiring in their efforts to carry out my every wish, and I am deeply sensible of their help and co-operation.

To the Government Department of Scientific and Industrial Research, I am indebted for the services of Miss Blackwood, who was generously placed at my disposal as a research assistant.

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VOLUNTARY MUSCULAR MOVEMENTS IN CASES OF NERVE LESIONS

By Prof. FREDERIC WOOD JONES, D.Sc.

When, after the experience of a few months of war, peripheral nerve lesions came to be treated upon what may be termed a wholesale scale, it was felt by many clinicians that their experiences were fast outrunning the amount of exact anatomical information obtainable in most of our text-books. In no connection was this state of affairs made more manifest than in dealing with those cases which demanded a precise knowledge of the action of living muscles in the human body. Our anatomical text-books gave the actions of the muscles, they also gave the innervation of these muscles, and the lines along which information for the clinicians was to be had, consisted in arguing that since a particular nerve has been divided, certain muscles will be paralysed, and therefore the actions carried out by these muscles will not be performed. The first stumbling-block—the lack of precise knowledge as to the arrangement of the motor fibres in mixed nerves, and the exact site of origin of branches to individual muscles—was soon largely rectified, but the question as to what action any living muscle can actually perform is, as it always has been, a difficult one to settle. Now, it has been within the experience of everyone who has come in contact with a large series of cases of nerve lesions that, at times, after the undoubted division of a motor nerve, the resultant paralysis has not been so great as would have been expected from a study of text-book anatomy. If it is taught in the text-books that a certain joint is bent by the action of a definite muscle, and this muscle is supplied by a definite nerve; then, when this nerve is divided, the expectation will be that since the muscle is paralysed, the action of bending the joint will not be performed. Not by any means uncommonly, this expectation is not fulfilled, for the patient continues to possess the power of bending the joint. Two explanations are at once forthcoming to account for this anomalous state of affairs. It is possible that, in this particular case, the nerve supply of the muscle is not that which is usually given in the text-books—that some other nerve sends branches to the muscle, and it is not paralysed at all. Or, it is possible that it is paralysed, and that some other muscle, or combination of muscles, may perform the action usually regarded as the exclusive function of this one. The first alternative has had its advocates, but we, as anatomists, need have little fear that a large revision of the text-book teaching upon the nerve supply of muscles will be necessary as an outcome of the study of war injuries. As a matter of fact, routine electrical testing upon the structures as they are exposed on

the operating table, should form a part of all operative work, and when this is carried out, the instances in which an appeal has to be made to abnormality of nerve supply, are reduced to a minimum. In all cases cited in this paper this procedure has been adopted. With regard to the second alternative, there is still a great deal of confusion. Much erroneous teaching has been put forward during the war, and many false conclusions arrived at in consequence of the deceptive nature of some of the voluntary movements possible after complete section of motor nerves. Testing voluntary movements is a business to be undertaken with a judicial mind, and at the best it is a difficult affair. It is easy to determine that a joint bends: it is by no means easy to determine beyond doubt what agent caused its bending.

It must never be forgotten that in testing voluntary movements, we ask the patient to perform some action;—we do not ask him to use certain muscles. The cortex of the patient neither knows nor cares of muscles, and his volition will therefore be effected by any agent capable—even in the lamest, and most halting way—of carrying out the volition. In some cases no agent having the power to perform the desired movement will be at hand, but at times some muscle may achieve a flicker in the right direction, or at times a perfect substitute for the paralysed muscle is prepared to take on the work. In any case, whatever beginning can be made at the business of reproducing the lost movement, it is probable that it will be steadily cultivated by the patient. The effort to perform a cortical volition by *any* agent is very remarkable, the most unlikely muscles will contract in an endeavour to effect the desired movement;—no man can flex his wrist with his platysma, but if the medical officer and the patient are both determined on doing their best, many men will attempt it. Among the muscles which will be called on in the attempt to perform a lost movement, are the antagonists of the desired movement, or any or every member of the groups of muscles having a general antagonism to the movement of volition. If, as a substitute for the paralysed flexors of a joint, the extensors of that joint be cortically activated, the volition of flexing will naturally not be attained; but if the extensors of some neighbouring joint be contracted, it is possible that a relative and passive flexion of the paralysed joint will result, and thus the volition may be achieved. Once the patient has learned this trick, the chances are that he will cultivate it, and the working of his perfected effort may be extremely difficult to detect. In the limits of the present paper, I have included "trick" movements, because although they do not throw much light upon normal muscular movements, they have led some observers to false assertions as to the incorrectness of orthodox text-book teaching.

In all the cases which are recorded here, and from which conclusions are drawn, the author has personally seen the condition of the nerve as exposed at the operation, and has checked the finding by the electrical tests. If a nerve is reported as divided, the statement means that the author has seen the complete severance in the continuity of the nerve, and witnessed the failure

of the exposed nerve to react to faradic stimulation. When movement is spoken of as being produced by the action of muscles, it must be understood that a real active movement of the part is achieved. In no case has a mere questionable flicker been reported as a voluntary movement. In all cases illustrated, the patient has been so arranged that the active movement has been carried out against the action of gravity.

A. *Complete division of the musculo-cutaneous nerve*

Paralysis of biceps and brachialis anticus. This is not at all a common lesion, and in only one of the cases that I have seen was the nerve actually

Fig. 1. Paralysis of biceps and brachialis anticus. Plexus lesion. Driver S.
Flexion of elbow produced by supinator longus.

severed by the passage of a projectile. In only one case of complete division (Pte. G. H. 8th R. Sussex, 2288), with the musculo-spiral intact, was there any evidence that the brachialis anticus retained any power of contraction. In this case the contraction was palpable but localised, and even in the most advantageous position it failed to produce any flexion of the elbow. In every case of paralysis of the biceps and brachialis anticus in which the musculo-spiral nerve was intact, the elbow was capable of immediate and strong flexion produced by the supinator longus (see fig. 1). Despite recent teaching, the supinator longus is always a flexor of the elbow joint. The

flexion of the elbow produced by the supinator longus is a powerful and precise action, and it is carried out with the hand in a useful working position. It is indeed often a matter of great difficulty to re-educate the patient in the use of the brachialis anticus and biceps, even after these muscles have perfectly recovered their voluntary contractibility.

B. *Complete division of the musculo-cutaneous and the musculo-spiral nerves*

Flexion of the elbow is performed by the pronator radii teres (see fig. 2). This flexion is nothing like so powerful, nor so complete, as that produced by

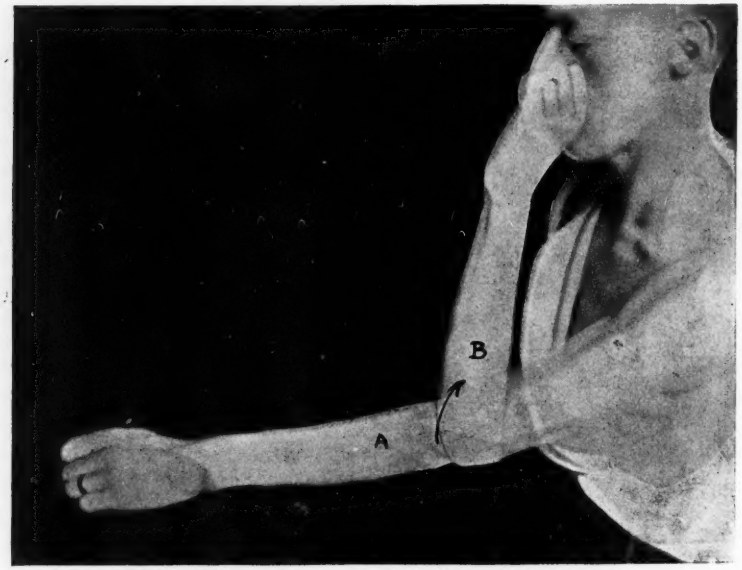

Fig. 2. Complete division of musculo-spiral and musculo-cutaneous. Lieut. L. B., gun-shot wound, left axilla, 24. iii. 18. Both nerves found divided, 22. iii. 19. *Flexion of the elbow produced by the pronator radii teres.*

the supinator longus. The action requires some cultivation by the patient, and even after a considerable interval the flexion may not be sufficiently complete to raise the hand to the mouth. In the case illustrated, the pronator radii teres was the only muscle which was used to perform the action, and the flexion produced was a forcible and useful movement when the forearm was maintained fully pronated.

The action of the biceps upon the elbow joint. Since there has recently been some attempt at revision of the established teaching concerning the action of the biceps as a flexor of the elbow joint; it is worth recording that apart altogether from the phylogenetic history of this flexor, and its undoubted

action as a flexor in the normal living human subject, its action is well seen in a very wide series of war injuries. Contracture of the elbow joint following a flesh wound limited to the biceps muscle is a common enough condition, and is comparable with the flexion of the knee so commonly seen following flesh wounds of the hamstrings. Cases of spasm of the biceps may follow prolonged splintage or slinging, and may be maintained with a hysterical basis for a period extending over years. (Case. Pens. G. C. 6 Glocs. 267306, shrapnel flesh wound middle R. Biceps—elbow flexed to right angle from 19. 7. 16 to 19. 5. 19. No other muscle or nerve involved.) Discrete contracture of the biceps fascia, without the involvement of any other structure, also produces flexion of the elbow.

C. *Complete division of the musculo-spiral nerve*

(1) Paralysis of the extensors of the wrist. Although "drop wrist" is such a classical symptom of musculo-spiral paralysis, and although it is so strikingly

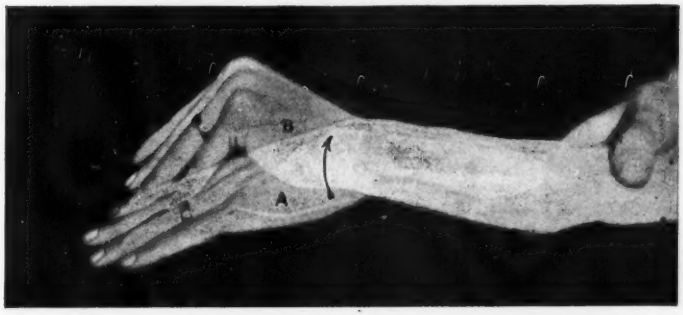

Fig. 3. Complete division of the musculo-spiral. Lieut. L. B., gun-shot wound, left axilla, 24. iii. 18. Nerve found completely divided, 22. iii. 19.
Extension of the wrist produced by flexion of the metacarpo-phalangeal joints.

complete in all cases of hysterical palsy, it not infrequently happens that a most astonishing power to extend the wrist against gravity persists in cases of complete division of the musculo-spiral nerve above the supply of all the extensor muscles. The production of this extension is a true "trick" movement, for it is done by pulling on the tendons of the extensor communis digitorum by flexing the metacarpo-phalangeal joints with the interossei. As the metacarpo-phalangeal joints are flexed, the digital extensors are tightened, with the result that the hand is forcibly extended at the wrist joint (see fig. 3). It will be readily understood that in all cases of trick movements the detection of the trick is far more difficult than would be supposed from an inspection of a photograph of the action, the patient often possessing a subtle power to manipulate one joint while the observer's attention is directed to a neighbouring one.

(2) Although in a complete musculo-spiral lesion the metacarpo-phalangeal joints cannot be extended, it must not be forgotten that the two terminal phalanges may be straightened from the flexed position by the action of the interossei. This action is, at times, mistaken for musculo-spiral activity, and it is especially liable to cause confusion if the hand be examined whilst supported on a splint.

(3) The movements of the thumb in cases of division of the musculo-spiral nerve have proved deceptive in a very large number of cases. It is by no means uncommon for the patient to possess the power of extension in the terminal joint, or at times to show ability to extend the thumb at the metacarpo-phalangeal joint. In by far the greater number of these cases, the action is produced as a trick movement, the terminal joint being first bent by the flexor pollicis longus and then, when flexion is released, extension is produced by the passive pull of the long extensor. But in other cases the movement

Fig. 4. Complete division of the musculo-spiral. Rfm. F. O., gun-shot wound, upper third right arm, 23. i. 17. Nerve found divided, 3. ii. 19. No response when tested on table.
Extension of the thumb in complete musculo-spiral paralysis.

is more complex. It will be noticed that when the thenar muscles act upon the thumb, extension of the terminal phalanx is normally produced. This extension may be brought about by the passive pull of the extensor pollicis longus against the ulnar adductors of the thumb in the normal action. Or it may be done by a direct pull upon the sesamoid, and so upon the head of the metacarpal bone and front of the metacarpo-phalangeal joint. This pull tends to bring the metacarpal forward, and so create a relative extension of the last two joints.

In the patient illustrated at fig. 4 this was probably the case, since upon the left side this patient had a complete division of the ulnar as well as the musculo-spiral and was quite incapable of producing a movement in his left thumb like that illustrated in his right. At times it is possible that the abductor brevis may produce an active pull upon the expansion to the long extensor

tendon: but I do not think these cases are at all common. All movements of extension produced by the thenar muscles may usually be detected by the wriggling motion imparted to the metacarpo-phalangeal joint of the thumb; but it is not true, as is so commonly taught, that extension of the terminal joint cannot be produced, in cases of musculo-spiral paralysis, when the thumb is abducted, unless the precaution be taken that this abduction and immobilization affects both the metacarpal and the first phalanx.

D. *Complete division of the ulnar nerve*

(1) Paralysis of the flexor carpi ulnaris is particularly difficult to test. It is more easy to appreciate the voluntary action of this muscle in producing the movement of ulnar deviation of the hand, than by attempting to estimate its condition during active flexion of the wrist. There are probably few muscles in the body in which the apparently simple task of estimating voluntary action by observation and palpation, is so exceedingly difficult.

(2) The action of the interossei in producing adduction and abduction of the digits may be simulated by other muscles, and great caution is needed before statements are made as to recovery in ulnar nerve lesions on the strength of the patient showing some ability to spread the fingers apart and close them

Fig. 5. Complete division of the ulnar. Lieut. A. W., gun-shot wound, left elbow, 30. vi. 18. Test, 10. iv. 19, no response in ulnar intrinsics.

Abduction of all the fingers produced by the action of the long extensors. A, is the resting position of the digits—B, the position to which they can be abducted by the long extensors.

together again. It is a commonplace that as we open our hands with the extensors our fingers tend to spread apart, and as we close our fist with the flexors, our fingers are adducted. The movement of abduction effected by the extensors may be perfected in a very remarkable manner and it is not uncommonly mistaken for interosseus action (see fig. 5). It is to be noted that in true

interosseus abduction the fingers are all spread from the middle finger as a centre, but in extensor abduction this does not hold good, for the fingers are spread as a fan is opened and in the case photographed, the 4th digit remains more nearly at rest than the 3rd. The only satisfactory method of performing the test for interosseus action is to isolate each finger, and test its power of adduction and abduction to and from the middle line without permitting the long flexors or extensors to come into play. There are two additional points to be noted concerning the abducting power of the extensors.

(3) The extensor minimi digiti proprius is an exceedingly powerful abductor of the little finger. Its action may easily be mistaken for that of the abductor minimi digiti: and the fact that the little finger possesses this added mechanism of abduction accounts for the permanently abducted position which the finger takes up even long after the recovery of a sutured ulnar nerve (see fig. 6).

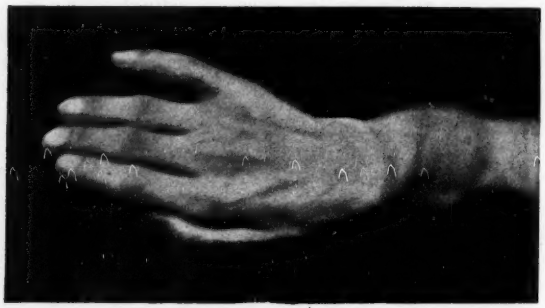

Fig. 6. Recovery after suture of the ulnar nerve; all ulnar muscles with completely recovered voluntary power.
Persistent abduction of the little finger caused by the action of the extensor minimi digiti and extensor communis digitorum.

(4) Although the extensor communis tendon to the index finger is able to produce abduction of the index in the general movement of extensor abduction, the extensor indicis proprius acts as a well-marked adductor. In the absence of any interosseus power, therefore, the index finger may be both adducted and abducted to and from the middle line (see fig. 7).

(5) The action of the long extensors upon the two terminal phalanges may prove a source of erroneous diagnosis. It has often been said that the action of the long extensors upon these two joints is but a feeble one; and recently it has been asserted very emphatically that not only have they no action whatever, but by the anatomical arrangement of their tendons, it is impossible that they should have any action. It is quite certain that the anatomical condition of the long extensor tendons, as properly displayed by dissection, is such as to permit extension of the two terminal joints of the fingers. It is equally certain that when the ulnar nerve is completely divided and the action of the interossei is entirely absent, the two terminal joints of the fingers

Fig. 7. Complete division of the ulnar nerve. Pte. W. R., gun-shot wound, left elbow, 17. iv. 18. Nerve found completely divided, 11. xii. 18. Test, 9. v. 19, no faradic or voluntary response in any ulnar muscle. Photo, May 1919.
Adduction of the index finger produced by the extensor indicis proprius. Abduction by extensor communis digitorum.

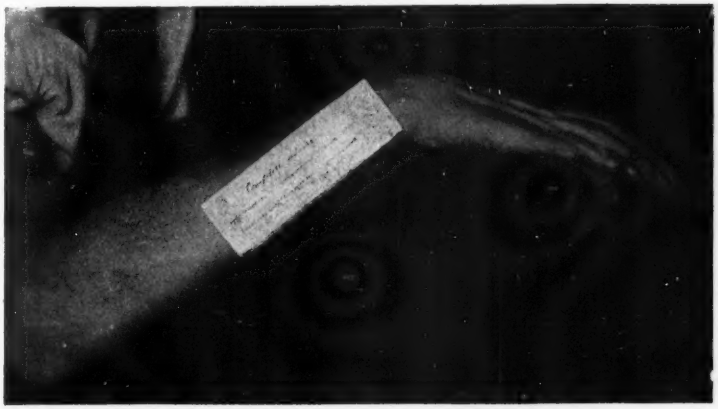

Fig. 8. Complete division of the ulnar nerve. Pens. C. H. H., gun-shot wound, right elbow, 21. x. 17. Nerve found completely divided, 26. iv. 19. Test, 26. iv. 19, no faradic or voluntary response in any ulnar muscle. Photo, May 1919.
Extension of the two terminal phalanges by the extensor communis digitorum.

can be extended by the action of the long extensors acting alone. This is not an abnormal action, it is one that can be witnessed in any case of division of the ulnar nerve, though the extension produced may not be so complete in all cases as in that illustrated at fig. 8.

(6) The statement that in complete ulnar lesions the metacarpo-phalangeal joints of the little and ring fingers cannot be flexed is, as a rule, incorrect. Although in the characteristic position of ulnar paralysis this joint in the little finger is extended, and the flexor digitorum sublimus has already produced a flexion of the first interphalangeal joint, nevertheless, a considerable degree of bending may be produced in the metacarpo-phalangeal joint by further action of the tendon of the flexor sublimus. In the ring finger, flexion of the metacarpo-phalangeal joint is readily produced by the flexor sublimus in cases of complete ulnar paralysis.

E. *Complete division of the median nerve*

(1) Several incorrect teachings concerning the failure to produce flexion in certain finger joints are current at the present time. The amount of paralysis that follows complete section of the median nerve is far less than would be imagined as the result of a study of anatomical text-books, and it is far less than that asserted by some observers of nerve injuries during the war.

(2) It is said that in cases of complete median interruption, the patient is unable to flex the second phalanges of any of the fingers. Flexion of the second phalanges, however, can readily be brought about by the flexor profundus *after* this muscle has bent the terminal joint. The second phalanges of minimus, annularis, and medius, can always be bent in complete median paralysis by the action of the intact flexor profundus (see fig. 10). The flexion produced is of a characteristic type, and may best be described as "winding up the finger."

(3) It is also asserted and emphasized by deductions from observations on the cadaver that the interossei cannot produce flexion of the metacarpo-phalangeal joints; these joints being bent by the action of the lumbricales only. This teaching is absolutely wrong, and it has led to the very incorrect diagnostic criterion that in median nerve paralysis the metacarpo-phalangeal joints of index and medius cannot be flexed. Every case of complete division of the median nerve has power to flex the metacarpo-phalangeal joints of these fingers, and the flexion in these cases is produced, as it is in the normal subject, by the action of the interossei, although, of course, the lumbricales assist in the action (see fig. 9).

(4) The common statement that the distal phalanges of index and medius cannot be flexed, needs very careful qualification. If the index finger be grasped, and the patient is told to bend the top joint of that finger only, no action of flexion is produced. If the same test be applied to medius, a definite flexion movement can usually be evoked. But if the patient is merely asked to bend the fingers, or especially if he is asked to make a fist, then some flexion of all joints

of all the fingers is produced. In some cases a very fair fist may be made in cases in which the median nerve is completely divided (see fig. 10). Evidently,

Fig. 9. Complete division of the median. Pte. C. W., gun-shot wound, left arm, 10. iv. 18. Median found divided, 17. vii. 18. No voluntary or faradic response in median muscles, 26. iv. 19.
Flexion of index and medius at the metacarpo-phalangeal joints.

Fig. 10. Complete division of the median. Pte. A. H., gun-shot wound, right arm, 21. iii. 18. Nerve found divided, 21. ix. 18. No voluntary or faradic response in median muscles, 12. v. 19.
Ability to make a fist with the median divided above the supply of the long flexors of the digits.

if the volition is a general one, the main action of the flexor digitorum profundus brought about by the route of the ulnar nerve is sufficient to produce a flexion of all the fingers. But if the volition is merely limited to the exclusive

median portion destined for the index finger, then no contraction of the muscle takes place.

(5) Flexion of the terminal joint of the thumb is sometimes possible in median nerve lesions in which the long flexor is paralysed. The flexion, though definite, is not complete, and is stamped by that characteristic inability to operate in the presence of any resistance which usually accompanies movements produced by relaxation of opponents.

(6) Flexion of the metacarpo-phalangeal joint of the thumb has been said to be impossible without the action of the muscles innervated by the median nerve: but the ulnar muscles inserted to the ulnar sesamoid are capable of producing this movement, and in this instance, as in the next two to be examined, we have an example of the almost utter impossibility of diagnosing lesions of the nerves supplying short muscles of the thumb merely by looking

Fig. 11. Complete division of the median. Pte. C. W., gun-shot wound, left arm, 10. iv. 18. Nerve found divided, 17. vii. 18. 26. iv. 19, no faradic or voluntary response in any median intrinsic muscle.
Opposition of the thumb in complete median paralysis.

at the movements of which the thumb is capable. Electrical tests and careful palpation of the thenar muscular mass are essential preludes to a diagnosis.

(7) It is best to state quite dogmatically at the outset that the complex combination of muscular movements which gives effect to the volition of opposing the thumb to the other digits, is often perfectly carried out in cases of complete division of the median nerve (see fig. 11). In performing this action, some muscle is needed to pull the metacarpal bone of the thumb in a palmar direction, another muscle is required to move the thumb towards the ulnar side of the palm, and to complete the process of perfect opposition some muscle is required to produce a rotation of the thumb. The extensor ossis metacarpi pollicis produces a forward movement of the metacarpal bone, and in the production of opposition in cases of median paralysis the part played by this muscle is generally apparent. When the thumb is pulled in a palmar direction, the adductor pollicis will produce the ulnar sweep, and,

with effective opposition from the extensor ossis, will also produce a deceptive degree of rotation of the thumb. In many cases in which the movement of opposition is quite perfect, that part of the adductor obliquus muscle which is inserted to the radial sesamoid effects a rotation not to be distinguished from true opponens opposition as in the case illustrated in fig. 11. Digital examination of the metacarpal of the thumb will reveal the atrophy of the opponens in these cases, but mere inspection of the movements produced may not be taken by any anatomist or any clinician as evidence of median recovery.

(8) The loss of the abductor pollicis in median paralysis is often extremely well compensated by the power of the extensor ossis metacarpi pollicis to pull the whole thumb in a palmar direction. A good deal of reliance has been placed on the "abduction test" in cases of median paralysis: but in a certain

Fig. 12. Complete division of the median. Nerve divided for pain, 20.ii.19. No recovery, 26.v.19.
"Abduction" movement of the thumb produced by extensor ossis metacarpi pollicis.

number of cases this spurious abduction brought about by a muscle innervated by the musculo-spiral nerve is a very well defined and forcible action, though naturally its range of movement is never so great as in that produced by the abductor brevis (see fig. 12).

F. *Complete paralysis of both median and ulnar nerves*

(1) It is in this condition that the typical "ape hand" is developed. The essential features of this hand are the flatness of the palm, and the rotation of the thumb in a direction opposite to that produced by the opponens (see fig. 13). The thumb ranges itself alongside the index finger with its palmar surface directed in a palmar direction, in the same manner as the remainder of the digits. It is rather curious that the production of this position

of the thumb is ascribed by Benisty[1] to the action of the adductor pollicis—a muscle which is of necessity paralysed in these cases.

The muscle which produces this movement in the thumb is the extensor pollicis longus which is thus, as regards rotation of the thumb, the opponent of the opponens.

Fig. 13. Complete division of ulnar and median nerves. Pte. J. B.
Typical position of the thumb produced by the rotating action of the extensor pollicis longus unopposed by the intrinsic thenar muscles.

Fig. 14. Complete division of both ulnar and median. Pte. A. B., gun-shot wound, right arm, 10. iv. 18. Both nerves found divided, 11. vi. 18. No recovery, 26. v. 19.
Flexion of the fingers produced by extension of the wrist.

(2) One very curious and deceptive action seen in some cases is that illustrated in fig. 14. Although all the finger flexors are completely paralysed, distinct and forcible flexion, which enables the patient to scratch with the finger nails, and to close the hand, is readily carried out. This trick action

[1] *Clinical forms of nerve lesions*, 1918, pp. 55 and 116.

is exactly the opposite to that mentioned in those cases of musculo-spiral paralysis in which the wrist may be raised by bending the fingers; for here the bending of the fingers is effected by raising the wrist.

(3) An action which has led to more confusion in diagnosis than probably any other, is that power of wrist bending which is normal to the extensor ossis metacarpi pollicis. The movement of the wrist produced by this muscle is illustrated in fig. 15, and in this case the action effected against gravity is a forcible one, although under these conditions its range is not very great.

G. *Nerve lesions of the lower extremity*

In the leg there are but few voluntary muscular actions which are likely to deceive, but it may be said at once, that if voluntary power is examined for with the patient lying on his back with his heel resting on the couch,

Fig. 15. Complete division of ulnar and median. Pte. A. R., gun-shot wound, left axilla, 19. vii. 18. Both nerves found divided, 13. xii. 18. No faradic or voluntary response in any median or ulnar muscle, 5. iv. 19.
Flexion of the wrist produced by the extensor ossis metacarpi pollicis.

almost any conclusion may be arrived at. The patient has only to push or to pull against his heel as a fixed point to produce movements of his foot in either direction; and this push or pull may be effected by any muscle capable of taking a leverage from the couch.

(1) The action of the peronei as elevators (dorsi-flexors) or depressors (plantar-flexors) of the foot has been somewhat debated. In the first place, the peronei belong to the external popliteal group of muscles and their normal action on the foot is to produce eversion. Eversion is itself a movement of greater possibilities in the position of dorsi-flexion. But it has often been said that anatomically the peronei—or some of them—are muscles which produce plantar-flexion. There is no doubt that in the normal condition the peronei act with their group, and come into play during dorsi-flexion of the foot. Suppose, however, the internal popliteal nerve is completely divided and the

calf muscles are paralysed, will a movement of plantar-flexion be produced by the peronei? In the great majority of patients there remains no power to depress the foot under these conditions, for the peronei, even if anatomically capable of producing plantar-flexion, cannot be dissociated in their action from the remaining muscles, supplied by the external popliteal, which produce dorsi-flexion. But, at times, the patient possesses the power of contracting the peronei without contracting the other external popliteal muscles;—he can dissociate the action of the peroneus group. In these cases plantar-flexion, and eversion is the result; and if the action be not carefully studied, it may be mistaken for evidence of internal popliteal recovery (see fig. 16). One might therefore say that normally the peronei were muscles which do not act upon the ankle joint, but which produce eversion of the foot usually in a position

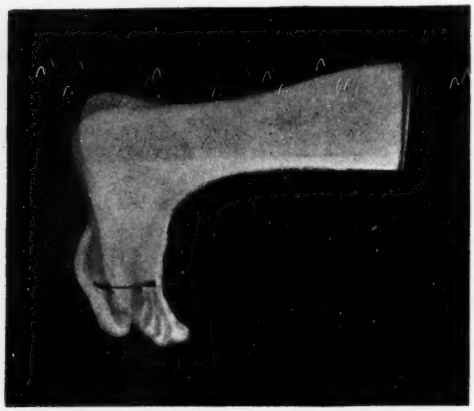

Fig. 16. Complete division of the internal popliteal; verified, 30. v. 19.
Action of the dissociated peronei muscles.

of dorsi-flexion, but that occasionally, in cases of internal popliteal paralysis, they may be dissociated by the patient from the remainder of their group and be used as plantar-flexors when they act alone. This is a case of the volition demanding plantar-flexion finding in some persons an agent not usually employed in this service.

CONCLUSIONS

The purpose of this paper is to emphasize the fact that estimating the condition of injured nerves by the study of the voluntary movements of which the patient is capable, is an extremely difficult, and at the best, somewhat uncertain business. That the re-education of muscles, in cases of nerve injury, is a matter requiring far more anatomical knowledge than is often brought

to bear upon it; since without proper care it will certainly result in the education of trick movements which, when perfected, are accepted as evidences of recovery. That much of the teaching upon muscular action which has been put forward from a study of nerve lesions during the war is erroneous.

Finally that anatomists should exercise great caution before authoritative sanction is given to teaching which may lead to false estimates of the damage done to nerves, and the recovery of nerves after operation; since on the one hand operation may be negatived or delayed, and on the other operative procedures which are futile may be encouraged, or legitimate operations may be estimated as having an unreal success. In either case that period which marks the transition from the sphere of activity as a serving soldier to that of useful civil employment may be very much prolonged. When, as during the war, the problem affected the welfare of thousands, it behoves anatomists to exercise an attitude far more judicial—far more critical—than has been evidenced up to the present time.

I wish to express my indebtedness to Major-General Sir Robert Jones and to Major Rowley Bristow for the opportunities for clinical investigation that form the basis of this paper.

SEXUAL DIFFERENCES IN THE SKULL

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More than a year ago one of us worked out the average contours of 30 male and 30 female, eighteenth century, skulls from the Clare Market district, though there was then no time to work out or call attention to the sexual points of difference between them.

As a matter of fact there was no way of being sure how far they were rightly sexed because few anatomists have the chance of testing their capabilities in this way on a series of skulls of known sex.

Still we propose to take the two series of tracings as a starting point and to see whether any of the differences between them are repeated in other series.

In the first place, on comparing the two norma verticalis tracings (fig. 3), it is evident that the female skull is shorter and broader in proportion than is the male, and it is no surprise to find that its cranial index is 77·5 while that of the male is 75·5. As it is obviously an important point to settle whether any definite allowance should be made for sex in comparing different groups of skulls we looked up the records of the other series of English skulls lately measured and found them as follows:

Hythe	♂ 79·9	♀ 81·9
Rothwell	♂ 76·3	♀ 75·8
Moorfields	♂ 75·5	♀ 75·0
Whitechapel	♂ 74·3	♀ 73·1

The results of this investigation were not very encouraging; Hythe showed the same preponderance of 2 per cent. in the female index noticed in the Clare Market series, but in the other three groups the males had a larger index than the females. We felt therefore that it was essential to get some material where the sexing was not the arbitrary work of an expert whose personal equation was unknown, even to himself, and we turned to the records of Anglo-Saxons because, as they are generally buried with male or female weapons and ornaments, there is much less chance of mistaking the sex than in later English burials.

22 male Saxons gave us an index of 74·3, and 23 females one of 75·3.

Later on, Dr Duckworth of Cambridge helped us very much by sending us records of 160 bodies from the dissecting room on which both the head

and the skull measurements had been taken and in which, of course, there was no doubt of the sex.

The cranial index of 120 male skulls was 75·8 and of 40 female 78·2.

As we were unable to get any more series the sex of which was definitely known except the series of soldiers at Millbank in which there were no females for comparison, we had recourse to the living head and measured 150 male medical students at St Thomas's Hospital and 150 female students at the Medical School for Women.

This, of course, brought us up against the allowance which it is necessary to make for the soft parts in comparing the living head with the bare skull.

Until lately craniologists have followed the example of Miss Lee in allowing 11 mm. for these, but Dr Gladstone found that a little over 7 mm. was sufficient, while Dr J. H. Anderson suggested 9 mm.

Our method of testing the thickness of the covering tissues was to run a needle through a thin disc of cork, the needle was then stuck into the scalp until it touched the bone, when the cork was moved down to the skin; then the needle was withdrawn and the distance between the cork and its point measured.

This method was so simple that a large number of records could be obtained in London post-mortem rooms in a short time and we soon had ample evidence that 8 mm. was a good allowance for the soft parts in both the length and breadth of the skull. This is the more satisfactory in that it is midway between Gladstone's and Anderson's results.

With regard to height, it is not enough to allow for the thickness of the tissues on the vertex and in the roof of the external auditory meatus, because in a dried skull the ear plugs of the auricular craniometer are in quite a different position to that they occupy with the soft parts in place; they are much nearer together in the skull and the removal of the soft parts may merely allow them to approach one another while their centres still occupy the centre of the canal. Another point which has to be taken into account is that the cartilaginous meatus is rising as it passes inward.

In practice we found that scraping the soft parts out of the bony meatus until the plugs could occupy the position they would take in the dried skull made a difference on the average of 1·5 mm. and this we attributed largely to the slope of the meatus. We would therefore suggest allowing 5·5 mm. for the difference in height between the living head and the dried skull, 4 mm. for the scalp and 1·5 for the meatus. This is rather less than Anderson suggests but is somewhere very near the average.

In practice it will be found that the change from the cranial to the cephalic index means an addition of 1 per cent.

Another comparison available was between the male and female patients in St Thomas's Hospital whom we may regard as representative of the modern migratory Londoner of the lower and lower middle class, while a still further one was between the male and female visitors to the British Association's

meetings as quoted by Dr Macdonell. These probably would represent pretty much the same class of society as the male and female medical students; that is to say, perfectly nourished individuals interested in intellectual occupations.

If we now tabulate the results of these (with the possible exception of the Anglo-Saxons) definitely sexed series we get the following:

			Excess of ♀ index
Anglo-Saxons	♂ (22) 75·9	♀ (23) 76·3	0·4 per cent.
London Medical Students	♂ (150) 78·7	♀ (150) 79·5	0·8 „
Cambridge Dissecting Room	♂ (120) 78·01	♀ (40) 79·6	1·6 „
London Patients	♂ (50) 77·7	♀ (50) 79·3	1·6 „

It seems therefore that all the material which has not been subjected to arbitrary sexing agrees in giving the female heads a higher index than the male by about 1 per cent., and if this ratio should be confirmed in the future we may have in it a useful method of checking the correctness of our endeavours in sexing unknown collections of skulls[1].

The next point is to determine whether the female skull has increased its index by decreasing its length or increasing its breadth in proportion to the male and for this the length and breadth averages are necessary.

	L.	Br.	L.	Br.
London Med. Students	♂ 193·4	152·3	♀ 185	147
British Association	♂ 198·1	155	♀ 185·6	148·3
Cambridge Dissecting Room	♂ 194·3	151·5	♀ 186	148
London Patients	♂ 193·3	150	♀ 182·4	144·7
Clare Market	♂ 196	150	♀ 186	146

In other words, among the London Medical Students the length of the ♀ head is 95·1 per cent. of that of the male while the breadth is 96·5 per cent.

In the British Association	length is	93·7 per cent.
„ „	breadth is	95·7 „
In the Cambridge Anatomy School	length is	95·7 „
„ „	breadth is	97·7 „
In the London Patients	length is	94·4 „
„ „	breadth is	96·5 „

It will therefore be seen that in all these separate groups the ratio of the breadth of the female is 2 per cent. nearer that of the male than is the length, or, in other words, that there is a 2 per cent. greater loss of length than of breadth in the female English skull compared with the male.

Having traced the sexual difference to the length it naturally became a question whether it might not be accounted for by the greater development of the frontal sinuses in the male and the only means of checking this which occurred to us was to take the ophryo-maximal measurements and see whether

[1] Since writing the above we are interested to note that Fleure and James found the same increase of the cephalic index in the female sex in Wales. *Journ. Anthrop. Inst.* 1916, p. 48.

there was the same proportional difference between the sexes that was noticed in the glabello-maximal; the argument being that, as the ophryo-maximal length only affects the brain containing part of the skull while the glabello-maximal represents brain and air, any difference in the proportion of the two lengths to the breadth must be due to a difference in the air containing part.

In the large series of skulls at Hythe which one of us measured (*Journ. of Anthrop. Inst.* vol. XXXVIII. p. 419) it was found that the difference between these two lengths was, on an average, 2 mm. for male skulls and nothing at all

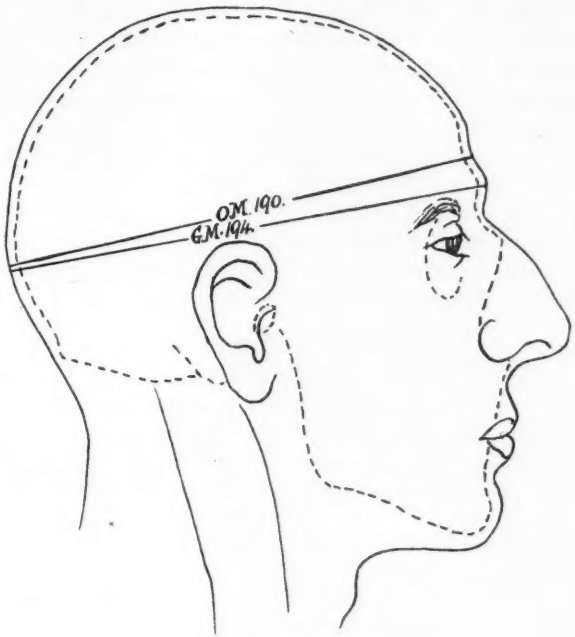

Fig. 1.

for the female. We have repeated the measurements on 100 patients in St Thomas's Hospital, 50 males and 50 females, with the same result.

Assuming that this difference is approximately accurate, we find that, if we deduct 2 mm. from the glabello-maximal length of the 150 St Thomas's Hospital male students' heads, the length of the 150 Women's School students is 96·65 per cent. of the St Thomas's length and the breadth 96·5 per cent. In other words that the female heads were 3·5 per cent. smaller than the male in both the antero-posterior and transverse diameter. This is exactly what we were looking for because on removing the 2 mm. due to air, the proportions between length and breadth become the same in the two sexes and so the cephalic index becomes the same.

When we came to the other series, however, the results were not so satisfactory from this point of view, but the simplest thing will be to tabulate the four sets of results.

	♀ shorter than ♂	♀ narrower than ♂
London Medical Students	3·5 per cent.	3·5 per cent.
London Hospital Patients	4·5 ,,	3·5 ,,
Cambridge Dissecting Room	3·3 ,,	2·3 ,,
British Association	5·4 ,,	4·3 ,,

From this it appears that the subtraction of 2 mm. from the male length does not equalize the proportions of length and breadth except in one series out of four. The other three agree in requiring another 1 per cent. removed from the male in order to equalize the cephalic index in the two sexes.

The amount is not great, but it is worth noticing, and our available material makes us think that the average English female skull is slightly broader, in proportion to its length, than the male even when the increased size of the air sinuses in the latter is allowed for.

One has, of course, to think whether there is any reason why the medical students should not have fallen into line with the other series, and the only one we can suggest is that they were all young adults in whom, perhaps, the sinuses were not as well developed as in the older groups.

On Checking the Sexing of Skulls

As all the different series of skulls in which the males and females were known agree in showing the female head as 2 per cent. broader than the male in relation to its length it appears that we have a check on the accuracy of the arbitrary sexing of those large series in which the sexes are not known.

Judged in this way the following results are interesting:

		♀ index > ♂	♀ index < ♂
(30 ♂ 30 ♀)	Clare Market	2 per cent.	
	Hythe	1·5 ,,	
	Moorfields		·6 per cent.
	Whitechapel		·3 ,,
	Rothwell		·5 ,,

The Clare Market and Hythe series therefore answer our expectations well enough, but the other three show the reputed males with a higher cephalic index than the females, a condition of things which is not in harmony with the evidence at present before us and makes us regard their accurate sexing as probably not very happy.

The Facial Index

On comparing the norma facialis tracings of the two sexes in the Clare Market series it will be seen that the males have an average length of 121 mm. from the nasion to the lower chin level against 116 mm. in the females while the greatest bizygomatic breadth is 129 mm. in the males against 123 mm. in the females. This means that the proportion of the length to the

breadth of the face or facial index is 93·8 in the male against 94·3 in the female. This, of course, is in the dried skull and we do not know any other collection of skulls, either accurately or tentatively sexed, with which to compare this because in all the collections we know the lower jaws are missing. We are, therefore, thrown back upon living faces with all the difficulties of adequate allowance for soft parts.

After careful examination of sections of faces we suggest 8 mm. as an ample allowance for the soft parts in the breadth and 4 for those in the length, and this would make the living Clare Market index 91·2 for the males and 91·6 for the females.

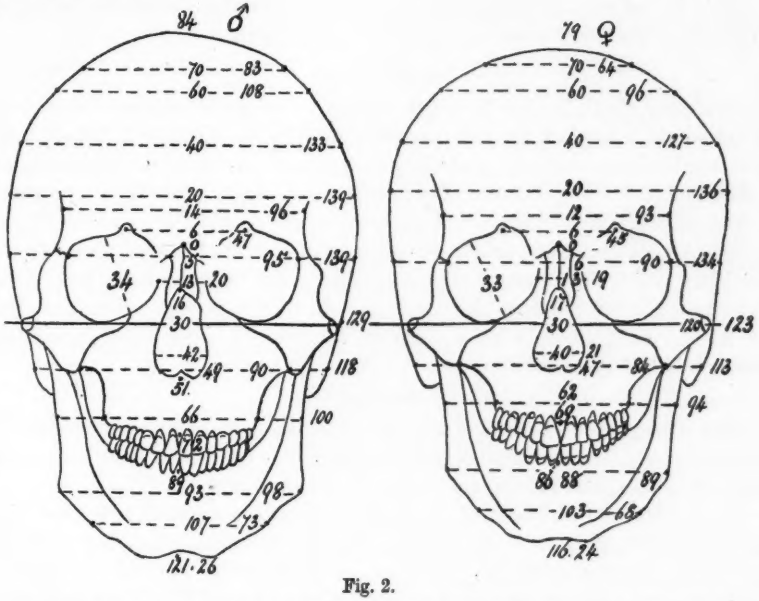

Fig. 2.

Against this we have to set 58 male students of St Thomas's Hospital with an index of 870 and 100 female students from the Women's School with one of 863, which means that while the Clare Market female facial index is practically equal to the male, the living female students' index is 99·2 that of the male students.

This makes us doubt whether any use can be made of the facial index for sexing purposes, and our work, so far, is negative from this point of view.

The Breadth-height Index

The difference in the appearance of the cranial vault is rather striking when the norma facialis of the two sexes is viewed side by side and suggests a difference in the breadth-height index. If this index is to be checked in the living head it will be necessary to use the auricular height which may be

ascertained by taking the height of the vertex above the Frankfurt plane and adding 6 for half the external auditory meatus.

This gives 120 mm. for the males and 115 for the females, and, when the maximal breadth is divided by it, the index is 84·5 ♂ and 83·3 ♀. This difference in the index means that the female skull has lost 4·2 per cent. of the male height but only 2·8 of the male width.

At present we have little material definitely sexed with which to compare this, but as far as 103 male and 25 female medical students go we find the proportion is the same because the male breadth-height index is 89·3 and the female 88·2.

This is the cranial index, not the cephalic, obtained after deduction of 8 mm. from the breadth and 5·5 mm. from the height.

Bimolar Width

Professor Keith has lately called attention to the diminution in the width of the palate in modern English compared with Saxon skulls; here we are only concerned with sex and it is striking how much narrower the female palate is than the male. The distance between the maxillary tuberosities in the males is 62 mm. while in the females it is 54 mm., and it will be noticed that the same line which joins the tuberosities is continued on to the lower jaw. In the maxillary width the female skull is 8 mm. narrower than the male, but in the wider mandibular width in the same line the female is only 6 mm. less than the male. Unfortunately we are unable to check this record at present on certainly sexed material.

Zygomatic Width

The Bizygomatic width or face breadth has been considered already in connection with the facial index and we now wish to consider it from the norma verticalis in connection with the width of the cranium.

In looking at this norma it is evident that the male skull is a good deal more phaenozygous than the female and the question arises whether the zygomata are more splayed in the male or whether the vault of the skull is fuller in the female in the anterior part of the temporal fossa. We shall probably get a better idea of this if we compare the bizygomatic width with the maximal skull breadth rather than with the inter-stephanic width.

If we do this we find that the zygomatico-maximal index or proportion of the zygomatic width to the maximal width is 90·9 per cent. in the male, and 87·0 per cent. in the female. This indicates that the zygomatic arch is distinctly wider in relation to the skull width in the male than in the female. We were able to check this in the male and female medical students in whom the male index was 89·7 per cent. and the female 88·5 per cent. These observations were made on 53 male and 100 female students.

Apparent tapering forward of the Skull

Apart from the difference in zygomatic width the male skull appears to taper away in the anterior temporal region much more than the female does;

in other words that the pterionic region in the female is fuller than in the male. A useful measurement is to our hand in the breadth taken a quarter of the way back along the length of the skull. This in the male is 115 and in the female 112. Contrasting these with the maximal width we get an index of 81 in the male and of 81·2 in the female.

This index suggests that the appearance of fulness is illusory and due to the feeble development of the zygomata in the female.

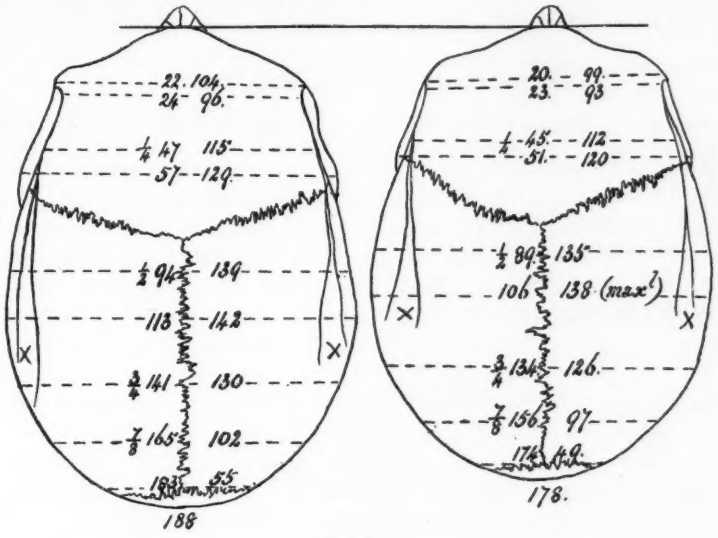

Fig. 3.

CONCLUSIONS

From the material at present at our disposal we have come to the following conclusions about the English skull.

1. That the female skull is shorter in proportion to its breadth than is the male by 2 per cent. and that this difference is not fully accounted for by the greater development of the frontal sinuses in the male.

2. That in those series of artificially sexed skulls in which this proportion is markedly departed from the sexing has probably been unsuccessful.

3. That the facial index does not differ in the two sexes.

4. That the female skull is lower in proportion to its width than the male, by from one to two per cent. when the auricular height is taken.

5. That the female skull is some 8 mm. narrower in the width of the palate than the male.

6. That the zygomatic arches are wider in proportion to the maximal breadth of the skull by 4 per cent. in the male than in the female.

THE ILEO-CAECAL REGION OF *CALLICEBUS PERSONATUS*, WITH SOME OBSERVATIONS ON THE MORPHOLOGY OF THE MAMMALIAN CAECUM

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The material on which this note is based consisted of three specimens of the South American monkey, *Callicebus personatus*, and one specimen each of *Dasypus sexcinctus*, *Tatusia novemcincta* and *Cyclothurus didactylus*, which were collected by the Percy Sladen Expedition to Brazil in 1913 and which were placed at my disposal by Professor J. P. Hill, to whom I desire to express my indebtedness and my thanks.

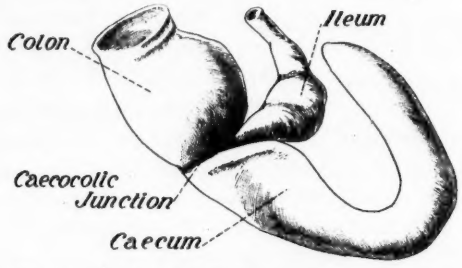

Fig. 1. Ileo-caecal region of *Callicebus personatus*. Ventral surface.

External appearances. In each case the commencement of the colon was distinctly dilated, although the length of gut involved was not constant, being 4 cm. long in two cases and 8 cm. long in the third—the "caecal colon" of Keith (1). The succeeding portion of the gut was in a state of tonic contraction for a distance of 8 cm. in the two former specimens and for 2·5 cm. in the third specimen. The term "caeco-colic sphincteric tract" has been suggested by Keith (6) for this portion of the large gut. From this point onwards to the anal canal, the colon showed a series of sacculations, each separated from its neighbour by a firmly contracted portion, varying from ·5 cm. to 1 cm. in length.

Only two taeniae coli could be made out. They were situated, the one on the dorsal surface and the other on the ventral surface of the colon near the mesenteric border, but their edges were not sharply demarcated.

The Caecum, which occupied the right iliac fossa, was demarcated from the colon by a circular depression which passed downwards and medially across the gut (fig. 1). In each of the three specimens it was distended and its capacity was rather greater than that of the stomach. In none did it contain gas. Its conformation was different in each case. In one (fig. 1), it was about 12 cm. long, and was curved to the left in a ∪-shaped manner. In another, it was 15 cm. long and formed a flat coil of one and a half turns. In the third, it was 16 cm. long and formed a spiral coil of one and a half turns, the commencement of the second turn of the spiral passing dorsal to the first turn. In each case it was clear that growth had been greater along the anti-mesenteric than it had been along the mesenteric border of the gut and that the coiled condition had resulted from an earlier ∪-shape.

The anterior and posterior vascular folds of Huntington (2) were present and the artery contained in the latter was in two of the three specimens the longer vessel and extended to the apex of the caecum.

In each case the caecum gradually tapered from its commencement to its apex, and in no case were taeniae coli distinct on its surface.

The Ileum terminated in the right iliac fossa by passing upwards and laterally into the medial aspect of the colon, where its entrance was marked on the surface by a V-shaped furrow (fig. 1). It was closely applied to the wall of the caecum.

Internal appearances. The mucous membrane of the commencement of the colon was smooth except on its dorsal wall where a few longitudinal corrugations were present.

The ileum protruded into the colon for ·5 cm. and its mucous membrane was thrown into ridges parallel to its long axis. The upper lip of the opening was quite distinct but the lower lip was not so salient owing to its relation to the caeco-colic valve.

The caecum was separated from the colon by a well-developed *caeco-colic valve*, annular in shape with a central opening and so placed that the plane of its aperture was directed upwards and medially. The valve was widest at the medial side of the gut, where it lay immediately below the termination of the ileum. The mucous membrane on both of its surfaces was thrown into radiating ridges (fig. 2), and, on the medial side, these ridges were directly continuous with the longitudinal ridges of the ileal mucous membrane. On the lateral side of the gut the caeco-colic valve was in the same plane as the upper lip of the ileo-colic valve, but, owing to the obliquity of its peripheral attachment, which corresponded to the depression on the outer surface (fig. 1), on the medial side it lay immediately below the lower lip of the ileo-colic valve. In this situation it hung downwards towards the caecum, presenting a spout-like appearance (fig. 2).

Over the ventral surface and along the anti-mesenteric border of the caecum, the mucous membrane was smooth, but longitudinal corrugations were strongly marked over the dorsal surface and along the mesenteric border.

At the base of the ∪ (fig. 1), two prominent transverse corrugations were present on the mesenteric border of the gut.

No lymphoid patches were recognisable in the ileo-caecal region on naked-eye examination.

Microscopical appearances. The upper or colic lip of the ileo-colic valve was, as is usual, covered on its outer surface with mucous membrane typical of the large intestine and on its inner surface with mucous membrane typical of the small intestine. The circular muscle coat of the latter was prolonged into the substance of the valve, but the circular coat of the large intestine ended abruptly at the base of the valve, where the longitudinal muscle fibres met and interlaced without becoming continuous with one another and without entering into the formation of the valve.

Sections through the lower or caecal lip of the ileo-colic valve also passed through the caeco-colic valve on the mesenteric border of the gut. The circular

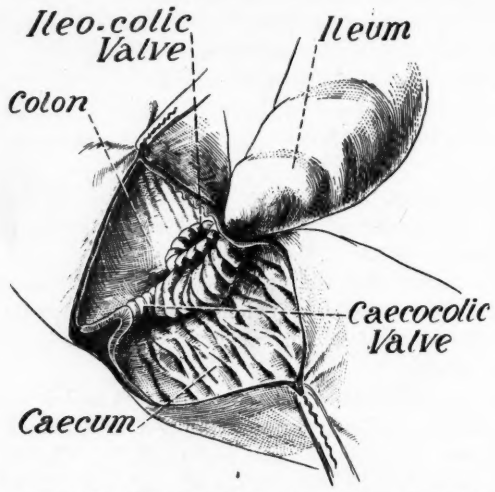

Fig. 2. Ileo-caecal region of *Callicebus personatus*. A window has been made in the wall of the gut so as to expose the ileo-colic and caeco-colic valves.

muscle coats of the ileum and caecum lay side by side, separated only by a few longitudinal fibres of the caecum and by some connective tissue, for some distance from the ileal termination. On separating from one another, that of the ileum entered the ileo-colic while that of the caecum entered the caeco-colic valve. The mucous membrane corresponded in its arrangement with the circular muscle coats. The villi disappeared at the apex of the lip of the ileo-colic valve and the mucous membrane, where it was associated with the circular muscle coat of the caecum, assumed the characteristic features of the large intestine.

The caeco-colic valve was covered on both colic and caecal surfaces by

mucous membrane typical of the large intestine, which was loosely connected with the underlying muscle. The entire thickness of the circular muscle coat of the colon passed into the substance of the valve, as did that of the caecum, so that the valve contained two layers of circular muscle fibres which became continuous near its free margin. These two layers carried in with them on their outer surfaces a fine layer of longitudinal fibres derived from the longitudinal muscle coats of the colon and caecum respectively. These fibres could only be traced into the middle of the valve and, thereafter, the two layers of circular muscle fibres were only separated by connective tissue (fig. 3).

The majority of the longitudinal muscle fibres of the colon were directly continuous with the longitudinal muscle fibres of the caecum.

The caecal wall showed no difference in structure throughout the whole of its extent, i.e. the mucous membrane near the apex was indistinguishable

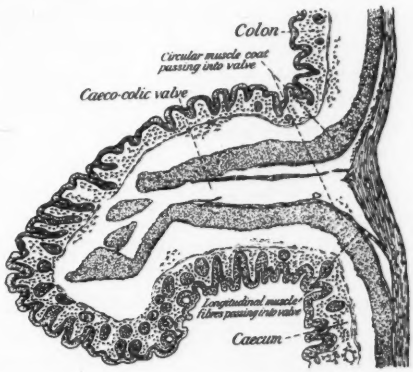

Fig. 3. Longitudinal section through the anti-mesenteric border of the gut at the junction of the caecum and the colon of *Callicebus personatus*, to show the structure of the caeco-colic valve.

from the mucous membrane of the rest of the caecum. Small nodules of lymphoid tissue were found in the submucous tissue but they were not more numerous near the apex than elsewhere.

Particular observations. The size of the caecum of *Callicebus personatus* relative to the size of the stomach and the presence of a competent caeco-colic valve constitute strong evidence that in this genus the caecum has a definite function to perform in connection with the process of digestion. The thickness of the circular muscle coat in the valve indicates that it acts as a powerful and efficient sphincter, and it is probable that the longitudinal fibres which enter into its constitution provide a muscular means of relaxation.

Fig. 3 shows clearly that the muscular core of the valve is not produced by a localised thickening of the circular muscle coat of the gut, but constitutes a true infolding of the whole thickness of that coat, a condition similar to that described by Sappey (3) in the spiral intestinal valve of Raja. Owing to the

obliquity of the peripheral attachment of the valve, many of the circular fibres which are found in it laterally, must, as they are traced medially, leave the valve and re-enter the wall of the colon, ultimately reaching the medial wall of the gut on the same level as the upper or colic lip of the ileo-colic valve. It would seem, therefore, to be not improbable that the contraction of these fibres approximates the lateral part of the caeco-colic valve to the upper lip of the ileo-colic valve, in this way causing the ileum to open into the caecum through the oblique inlet of the former. As already pointed out, the medial part of the caeco-colic valve is in intimate relation with the lower lip of the ileo-colic valve and its spout-like appearance suggests that the contents of the ileum may pass directly into the caecum.

The condition of the vascular folds of the caecum corresponds to what Huntington (2) described for the closely allied *Ateles ater*, namely that either the ventral or the dorsal fold and its contained artery may be the longer. It may be stated that the external appearances of the ileo-caecal region of *Callicebus personatus* and *Ateles ater* are very similar, but I have not had an opportunity of examining the internal and microscopical appearances of the latter.

As compared with the ileo-caecal region of *Callicebus personatus*, the condition found in the old-world monkey presents some manifest differences.

In a specimen of *Cercopithecus aethiops* which I examined, the stomach possessed a capacity eight or ten times greater than that of the caecum, which was, relatively, much smaller than the caecum of *Callicebus personatus*. The shape of the caecum in all the old-world monkeys is attributable to the fact that growth along the anti-mesenteric border of the gut has been in excess of the growth along the mesenteric border. Thus, in *Cercopithecus aethiops*, the caecum is ∪-shaped.

In all the old-world monkeys, the proximal part of the caecum is sacculated and these sacculations—produced in the same way as the sacculations in other parts of the colon—are separated from one another by deep furrows, which do not, however, pass completely round the gut, being absent at the mesenteric border. It follows that taeniae coli are well marked on the caecum in its proximal part. In *Callicebus personatus*, on the other hand, the sacculations are absent and the taeniae coli are not distinct.

In the old-world monkeys the terminal tapering of the caecum is abrupt, unlike the condition found in *Callicebus personatus*, but the diminution in calibre is not sufficient to justify its identification as a vermiform process.

The arrangement of the peritoneal folds in *Callicebus personatus* has been described on p. 67. In *Cercopithecus aethiops* the intermediate non-vascular fold is very well developed and forms a large triangular fold which occupies the angle between the terminal part of the ileum and the medial wall of the proximal part of the caecum. The anterior and posterior vascular folds, however, are very short so that the vessels they contain run practically on the gut wall.

In the specimen of *Cercopithecus aethiops* which I examined, the ileo-colic

valve was found to be directed tailwards, i.e. towards the caecum, and the terminal part of the ileum passed posteriorly and laterally into the colon. The specimen had been preserved in formalin and I believe that the condition was probably brought about by post-mortem and abnormal muscular contraction. At the same time it is clear that the particular muscular contraction which produced the condition after death may be able to produce the condition during life.

In the interior of the caecum of *Cercopithecus aethiops*, the furrows separating the sacculations on the outside formed definite folds containing circular muscle fibres. These folds may have acted as a sphincter for the caecum, but they were not continued all round the gut; they were produced by the difference in length between the longitudinal and the circular muscle coats; and they did not constitute a true caeco-colic valve.

If the condition of the ileo-caecal region of the new- and old-world monkeys be compared with the condition found in the anthropoid apes, it will be found that the increased growth along the anti-mesenteric border of the caecum is the most striking characteristic which all three groups possess in common.

The small size of the caecum relative to the stomach, the possession of definite taeniae coli and the corresponding caecal sacculations, and the absence of the caeco-colic valve are characters which the anthropoid shares with the old-world monkey.

On the other hand, the anthropoid differs both from the old- and the new-world monkeys in possessing a vermiform process. It also possesses both an intermediate non-vascular ileo-caecal fold and a well developed dorsal vascular fold[1].

It will be seen, therefore, that so far as the ileo-caecal region is concerned, the old-world monkeys are much more closely allied to the anthropoids than are the new-world monkeys.

It may be of some interest to point out that, as regards both the caecum and the caeco-colic valve, *Tarsius tarsius*, which Wood Jones (14) excludes from the Lemurs, closely resembles *Callicebus personatus*.

General observations on the mammalian ileo-caecal region. In human anatomy, the term caecum is used to denote that portion of the large intestine which lies on the proximal side of the ileo-colic valve. In comparative anatomy, the term is not always used to describe the same morphological entity. The caecum of the monkey corresponds exactly to the human caecum, but the caecum of the rabbit, the horse and some other mammals includes, in addition, the proximal part of the colon proper. This difference is not always borne in mind, but Keith (6) believes that the proximal part of the colon proper should be regarded as functionally part of the caecum and he terms it the "caecal colon." He has indicated that he considers that the "caecal colon"

[1] The morphology of these folds is fully discussed by Huntington (2).

is morphologically the primitive vertebrate caecum and that the diverticular blind end appears at a later stage in phylogeny.

In the present paper consideration is being restricted to the morphology of the *caput caecum coli* of human anatomy, and I would be content to draw attention to the risk of confusion in nomenclature and to point out that the "caeco-colic valve," which Sisson (4) describes in the horse, is not identical with the caeco-colic valve of *Callicebus personatus*.

The frequent occurrence of a competent caeco-colic valve is overlooked by Chalmers Mitchell (5) when he makes the following statement: "The normal caecum of mammals, however, always appears to be a forward continuation of the hind-gut, the one cavity being directly continuous with the other in the simplest fashion, except in those cases in which it is slightly complicated by vestiges of the presence of the second caecum of an original pair." It is not possible to regard the caeco-colic valve as a vestige of the presence of the second caecum of an original pair, even if one agreed with the author in his view that the primitive mammalian caecum was a paired structure. When it is remembered that the caeco-colic valve is a true sphincter of the caecum, that amongst mammals it is sometimes present, sometimes replaced by an intra-colic valve, and sometimes completely absent it will be evident that its value as an aid in studying the morphology of the caecum is by no means negligible.

In opposition to currently accepted ideas, Keith (6) has put forward the view that the human caecum is not in a state of retrogression. He regards the commencement of the colon, which is usually found to be dilated, as a feeding chamber for the caecum, the passage of the chyme being effected by anti-peristaltic waves, which Cannon (7) and Barclay Smith (8) have described. Keith points out that the portion of the colon immediately beyond the dilatation is very commonly found tonically contracted in mammals and in birds, and he looks upon it as a sphincter for the caecum and "caecal colon." Consequently he has suggested the term "caeco-colic sphincteric tract" to denote it and he believes that, in man, the upper part of the ascending colon represents this tract and functions as a sphincter for the human caecum. He draws attention to Berry's (9) work on the vermiform process in support of his view that the human caecum is an actively functioning part of the alimentary canal.

Annular valves, very similar to the caeco-colic valve of *Callicebus personatus*, are found in the alimentary canals of many fishes and reptiles, and are clearly very primitive in type, but they are none the less competent and efficient in their action. Many of Keith's observations were made on the rat and he has himself referred to the presence of a caeco-colic valve which he has figured. He does not explain, however, why, in the presence of a competent valve, a "caeco-colic sphincteric tract" should be necessary, nor does he explain why, if a sphincter is required, a tonically contracted tube should take the place of a primitive annular valve. The "caeco-colic sphincteric tract" would appear to be destined, like the oesophagus and the human de-

scending colon, to act as a passage for the rapid conduct onwards of incoming contents, and not as a sphincter.

Huntington (2) has drawn attention to the fact that "representatives of all the main types of ileo-colic junction are found within a very limited zoological range, as within the confines of a single order...differences in the method of nutrition have impressed their influence on the structure of the alimentary canal and have led to the evolution of varying and divergent types of ileo-colic junction." This is an indication that the possibilities of variation are limited, and I believe that they are very much fewer than Huntington lays down. Asymmetry in origin and asymmetry in growth are the outstanding characteristics of the mammalian caecum, and I believe that the primitive mammalian caecum was asymmetrical, i.e. a diverticulum derived from the anti-mesenteric border of the colon just beyond the ileal termination, such as is found in some reptiles, e.g. *Pseudemys elegans*, *Eunectes marinus*, etc. As the caecum enlarged and its functional activity increased, a caecal sphincter was developed. Further caecal progress necessitated the redistribution of, or increase in, the lymphoid tissue, with the consequent appearance of the vermiform process. Variations of diet led to retrogressive changes in form. Retrogressive changes at an early stage may account for the complete absence of the caecum in *Dasyurus viverrinus*. Retrogressive changes at a later stage may account for many of the reduction forms found in carnivora. Finally, retrogressive changes imposed on the most advanced form may account for the reduction in size accompanied by the retention of the vermiform process found in the wombat, the anthropoid apes and man.

Wood Jones (14) has recently put forward a somewhat unorthodox view of the morphology of the caecum. "The human vermiform appendix," he says, "although usually regarded as a particularly degenerated rudiment, is strangely like that of such simple creatures as some of the pouched animals of Australia, and the very different structure found in the monkeys is most likely a specialisation from a primitive condition which is retained in man." From this one might with some justice infer that the author believes that the simpler the animal, the more primitive the type of the caecum, but, as Huntington has shown, all the main types are to be found within the limits of a single order. The conception that such a caecum as that of *Callicebus personatus* or of *Cercopithecus aethiops* has been derived from a condition similar to that found in man and the anthropoid apes is one for which I am unable to find any supporting evidence. On the other hand, I have tried to show that the vermiform process is present in two types of caeca. In the one, the caecum is relatively large and obviously plays an important part in the digestive process and this increased functional importance demands a redistribution of the lymphoid tissue, which is manifested by the presence of the vermiform process.

In the other, the caecum is relatively small, it possesses no true sphincter, its wall is sacculated—a common condition in large, actively functioning caeca but uncommon in relatively small caeca, which do not possess a vermiform

process—and its general characters are such as to suggest strongly that it is a reduction stage of the first group.

Retrogressive changes necessarily are associated with loss of function and the caecal loss of function will be indicated in the first place by the disappearance of the sphincteric valve.

I therefore conclude that, in the determination of the phylogeny of a given caecum, the condition of the caeco-colic valve is of the greatest importance.

In putting forward this suggestion as to the primitive mammalian caecum, I am aware that it is in agreement neither with the conception of Huntington (2) nor yet with that of Chalmers Mitchell (13). The former refers all mammalian caeca to a primitive vertebrate type with no caecum, and he derives the various types found to-day in different ways from a condition similar to that found in *Echelus conger*.

Chalmers Mitchell (13) believes that the single mammalian caecum is the persistent member of a primitive pair of caecal appendages, homologous with the paired caeca of birds. He compares the paired caeca of birds and the paired caeca of the little ant-eater, *Cyclothurus didactylus*—which are both laterally placed—with the paired caeca of *Petaurus sciurens*, in which the large caecum is anti-mesenteric in position and the (?) vestigial caecum is connected to the mesenteric border of the gut, and he states that any anatomist would agree that the structures involved are the same.

This statement would only be justified if the author had brought forward evidence to show how caeca, which were previously lateral in position, came to be situated on the anti-mesenteric and mesenteric borders of the gut, and, in the absence of such justification, one cannot concede that the paired lateral caeca of *Cyclothurus didactylus* are identical with the so-called paired caeca of *Petaurus sciurens*.

If, therefore, we exclude the paired caeca of *Petaurus sciurens* and other forms where the larger structure—usually accepted as the caecum—is anti-mesenteric in position, there still remain certain mammals which have been described by Flower (10), Owen (11) and other observers as possessing paired lateral caeca. The list includes the armadilloes, *Dasypus sexcinctus*, *Dasypus villosus* and *Tatusia novemcincta*, the little two-toed ant-eater, *Cyclothurus didactylus*, and the *Manatee* (Chalmers Mitchell).

The *Manatee* possesses a bifid caecum, springing from the anti-mesenteric border of the gut, and can be excluded as an example of the paired lateral caeca.

In *Tatusia novemcincta*, the condition at the ileo-colic junction is described differently by different authors. Huntington cites it as an example of the symmetrical type of ileo-colic junction, with median transition of the ileum and, although he does not definitely make the statement, it can be inferred that he, like Flower (10), regards the caecum as being absent. Chalmers Mitchell on the other hand describes the same animal as possessing small paired globular caeca. Both these authors agree in believing that the "paired lateral caeca"

of *Dasypus sexcinctus* and *Dasypus villosus* constitute an advanced stage of the condition found in *Tatusia novemcincta.*

Examination of the ileo-colic junction of Tatusia, when the gut is empty, is sufficient to satisfy the observer that growth along the anti-mesenteric border of the commencement of the colon has been definitely greater than it has been along the mesenteric border (fig. 4). Further, the longitudinal muscle coat of the ileum passes continuously on to the anti-mesenteric border of the colon and there constitutes a definite taenia coli. This does not occur on the lateral aspects of the ileo-colic junction, and I believe that the condition represents a well-marked transition stage between the condition where the ileum is in direct linear continuity with the colon, and the condition which Huntington describes as the right-angled type of ileo-colic junction. I regard the dilatation on the anti-mesenteric border of the commencement of the colon as the true caecum. When the colon of Tatusia is artificially distended the lateral wall of the commencement of the colon tends to bulge, and these two bulgings are separated from one another by the anti-mesenteric taenia coli already referred to. These bulgings are regarded by Chalmers Mitchell as paired lateral caeca, but I prefer to regard them as the first stage in the production of a bifid caecum.

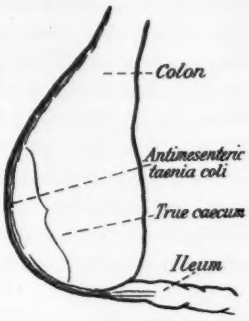

Fig. 4. Ileo-caecal region of *Tatusia novemcincta*, ventral surface showing anti-mesenteric taenia coli and asymmetrical ileo-colic junction.

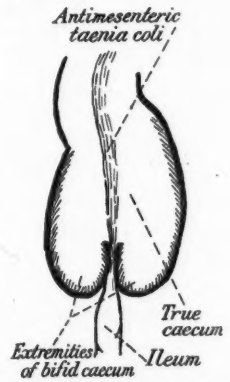

Fig. 5. Ileo-caecal region of *Dasypus sexcinctus* showing anti-mesenteric aspect with well-marked taenia coli separating the two extremities of the bifid caecum.

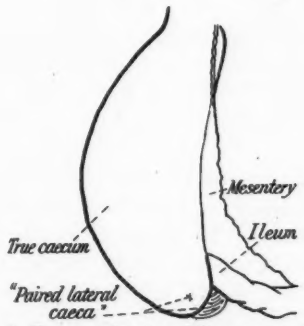

Fig. 6. Ileo-caecal region of *Dasypus sexcinctus* showing asymmetry which indicates the true caecum.

This view is strongly confirmed by the condition found in *Dasypus sexcinctus.* In this animal the anti-mesenteric taenia coli and its continuity with

the longitudinal muscular coat of the ileum are very striking (fig. 5). The colon is asymmetrically dilated at its commencement—the true caecum (fig. 6)—but further growth of the anti-mesenteric border of the gut has been modified, because the taenia coli has not kept pace. As a result *Dasypus sexcinctus* possesses "paired lateral caeca" which I regard as a typical unpaired caecum with a bifid extremity, and a modification of this caecum may, with justice, be believed to be the origin of the bifid caecum of the *Manatee*.

There remains for consideration the condition found in the little two-toed ant-eater, *Cyclothurus didactylus*, of which Hunter (12) says: "There are two caeca as in birds." Flower's (10) description is as follows: "The colon is short and is very remarkable for having at its commencement a symmetrically disposed pair of short caeca, narrow at the base, and rather dilated at their terminal blunt end, and communicating with the general cavity by very minute apertures."

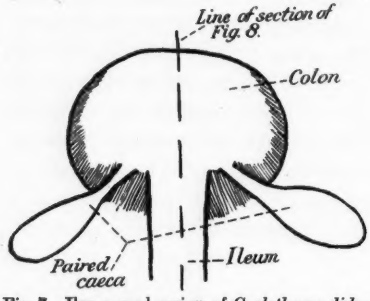

Fig. 7. Ileo-caecal region of *Cyclothurus didactylus*, ventral view showing the "paired lateral caeca."

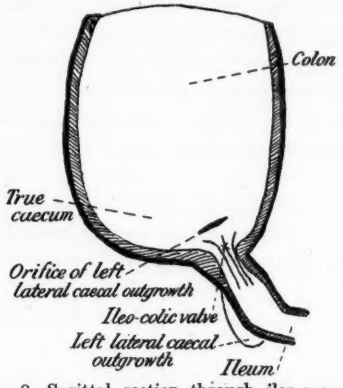

Fig. 8. Sagittal section through ileo-caecal region of *Cyclothurus didactylus* along line shown in Fig. 7. The asymmetrical ileo-colic transition is shown and the position of the true caecum is indicated.

Huntington (2) classes it as a more advanced stage of the condition found in *Dasypus sexcinctus*, but the caeca of these two animals show very striking differences. In Dasypus, as already noted, the paired caeca are separated from one another only by the anti-mesenteric taenia coli. In Cyclothurus, their attachments are very widely separated (fig. 7). In Dasypus, the caeca are of a size in conformity with the size of the colon, whereas in Cyclothurus they are relatively very small. In Dasypus, the caeca are widest at their connection with the colon; in Cyclothurus, they are very narrow at their colic ends, but dilated and bulbous at their blind extremities, a curious condition to which Flower (10) has drawn attention.

A sagittal section through the ileo-colic junction of Cyclothurus (fig. 8) shows the same asymmetrical transition as has been already pointed out in

Tatusia novemcincta, and a similar degree of increased growth along the anti-mesenteric border of the colon.

Transverse sections through the stalk or proximal part of the caecal outgrowth show that the mucous membrane is thick and vascular and that the lumen is relatively small. In the distal two-thirds, the lumen is much larger but the mucous membrane is not so thick. A complete longitudinal muscular coat is present throughout, as in the vermiform process of other animals. Unfortunately, in the specimen examined by me the material had not been fixed with a view to microscopical examination, and I am therefore unable to describe the appearance of the mucous membrane, beyond saying that it appeared to conform to the type usually found in the caecum.

Consideration of the differences which have been enumerated above leads me to regard the paired lateral caecal outgrowths as new formations and the dilatation at the commencement of the anti-mesenteric border of the colon (fig. 8) as the morphological caecum.

It is clear therefore that the paired caeca can be explained in such a way as to bring them into line with other mammalian caeca and that they do not constitute an insurmountable obstacle to the acceptance of the views which have been put forward in this paper.

CONCLUSIONS

1. The caecum of *Callicebus personatus* is an actively functioning part of the alimentary canal.

2. The caeco-colic valve is the true caecal sphincter.

3. Where the functional caecum does not correspond to the morphological caecum, e.g. in the horse, the rabbit, etc., the caeco-colic valve is replaced by an intra-colic valve.

4. The human caecum, which possesses no competent caeco-colic or intra-colic valve, is in a condition of retrogression.

5. The primitive mammalian caecum was an asymmetrical structure derived from the anti-mesenteric border of the colon immediately beyond the ileo-colic junction by increased growth over a localised area.

6. The paired lateral caeca of *Dasypus sexcinctus* and *Dasypus villosus* are regarded as the extremities of a bifid caecum.

7. The paired lateral caeca of *Cyclothurus didactylus* are new formations and do not correspond to the morphological caecum.

At the same time, one recognises that much valuable information, which has still to be obtained with regard to the comparative embryology of the caecum, is not yet available and that it may therefore be necessary to modify one's views in the light of subsequent knowledge.

I desire to express my thanks to Mr G. L. Birbel, who is responsible for figs. 1 and 2, and to Miss Muriel Sutton, B.Sc., who is responsible for fig. 3, for the care and trouble which they have taken over these drawings.

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ON THE DEVELOPMENT OF THE LARYNGEAL MUSCLES IN SAUROPSIDA

By F. H. EDGEWORTH, M.D.

In a paper published in 1916 I showed that in the pig the laryngeal muscles, other than the Crico-thyroid, are developed from the Constrictor oesophagi. In this paper evidence is given that the laryngeal muscles of the Sauropsida have a similar derivation.

Reptiles. The laryngeal cartilages of Reptiles (vide Henle and Göppert) consist of a cricoid, and two arytenoid cartilages articulating, or continuous, with it. The musculature consists of a Dilatator laryngis and a Constrictor laryngis. Laryngei are present in some cases.

These muscles were considered by Göppert (1899) to be homologous with those of Amphibia, and like them, to be derived from branchial muscles.

As far as I know, no description has hitherto been given of the development of the cartilages or of the muscles.

Hochstetter (1908) stated that in Reptiles (Emys lutaria, Anguis fragilis, Tropidonotus, Lacerta agilis) the lungs are developed from paired lateral or ventro-lateral grooves of the epithelial lining of the oesophagus. At their anterior ends they communicate by a transverse bifurcation groove, whilst in front of this and continuous with it a median ventral groove develops. The pulmonary sacs grow backwards from the hind ends of the pulmonary grooves. The bifurcation and branchial grooves are folded off from the oesophagus, from behind forwards.

Schmidt (1913) stated that in embryos of Calotes, Mabuia, and Ptychozoon, the lungs are developed from the oesophagus, as paired diverticula at the junction of its lateral and ventral walls. The trachea is developed later, behind the branchial region, as a shallow median groove in the floor of the oesophagus. It extends backwards and soon joins the transverse bifurcation groove which unites the pulmonary diverticula. In Calotes and Mabuia, though most marked in the former, there are two tracheal grooves, of which the left becomes the permanent groove, whilst the right gradually disappears by being taken up into the left groove. The tracheal groove subsequently extends forwards into the pharyngeal region, the epithelium in the median line of the floor of the pharynx thickening into a plate. Meanwhile the separation of the trachea from the oesophagus proceeds cranially, right up to the solid epithelial plate. The breaking through of the tracheal lumen into the pharynx was not observed—it occurs later. The solid epithelial plate corresponds in position to the larynx.

The development of the laryngeal muscles was followed in Chrysemys marginata and Tropidonotus natrix.

In a 6 mm. embryo of Chrysemys (figs. 1–3) the open tracheal groove extends from the bifurcation groove, 180 μ behind the 5th gill-clefts, forwards to 80 μ behind them. In front of this the oesophagus has a more oval shape. The oesophagus and tracheal groove are surrounded by cells of uniform appearance and no indication of oesophageal or laryngeal muscles is visible.

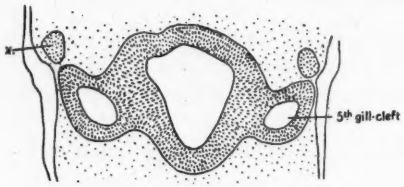


Fig. 1.

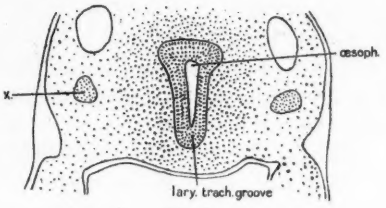
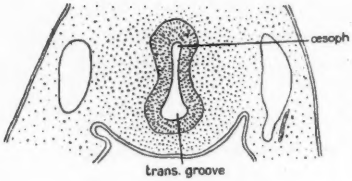


Fig. 2.



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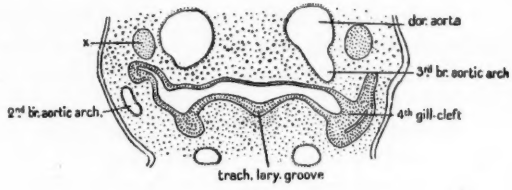

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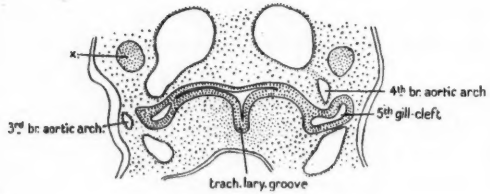

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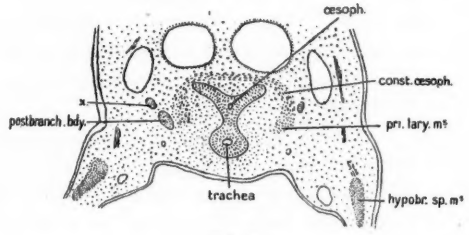


Fig. 6.

In an embryo of 7 mm. (figs. 4–6) the tracheo-laryngeal groove begins 140 μ behind the 5th gill-clefts, and is continued forwards to the level of the 4th gill-clefts; it is a deep groove in the oesophageal region and at the level of the 5th gill-clefts; it then becomes wider and shallower and is barely marked at the level of the 4th gill-clefts. The trachea behind the bifurcation groove and the tracheo-laryngeal groove are surrounded by aggregated mesoblast cells—the first indication of the laryngo-tracheal skeleton. The forepart of the oesophagus is surrounded, dorsally and laterally, by the ∩-shaped primordium of the Constrictor oesophagi and laryngeal muscles.

In an embryo of 8 mm. (fig. 7) the primordium of the laryngeal muscles has separated on either side from the Constrictor oesophagi. It extends from 170 μ behind, to the level of, the 5th gill-clefts. The recurrent laryngeal nerve passes towards it.

In an embryo of 9 mm. (figs. 8–10) the tracheo-laryngeal groove extends from 100 μ behind the 5th gill-clefts to the level of the 4th gill-clefts. The tracheal lumen is continued forwards to the level of the 5th gill-clefts. The primordium of the laryngeal muscles extends from 140 μ behind the 5th gill-clefts to the level of the 4th gill-clefts.

From this time onwards the increasing curvature of the embryo made another method of measurement necessary. In an embryo of 8·1/2 mm. crown-rump length—slightly more advanced than one of 9 mm. in total length—there is but little change. The tracheo-laryngeal groove begins 50 μ behind, and the laryngeal-muscle-primordium 90 μ behind, the 5th gill-clefts.

In an embryo of 12 mm. crown-rump length (figs. 11–14) the trachea has altogether separated from the oesophagus, so that the laryngeal epithelium is continuous only with that of the branchial s. pharyngeal region, from the level of cornu branchiale i to that of the cornu hyale. The laryngeal muscles lie solely in the branchial s. pharyngeal region. Their primordium, on each side, has separated into the lateral half of the Constrictor laryngis and the Dilatator laryngis. The former meets its fellow in the mid-dorsal and mid-ventral lines. The latter lies external to the Constrictor.

In an embryo of 15 mm. (figs. 15–16) crown-rump length the ventral surface of the Constrictor is attached to the Basibranchiale. The cricoid and arytenoids form a continuous, slightly chondrified mass, which is continuous posteriorly, with the tracheal skeleton.

In Tropidonotus the younger embryos have a cork-screw form so that measurements of length were not possible, and the stages described are arbitrarily named.

In stage (i), the earliest available (figs. 17–20), the continuity of the tracheo-laryngeal with the oesophago-pharyngeal epithelium extends from 30 μ behind the 5th gill-clefts to the 4th gill-clefts. The primordium of the laryngeal muscles, just separated from the Constrictor oesophagi, extends from 90 μ behind to the level of the 5th gill-clefts. The recurrent laryngeal nerve passes to its hind end.

In stage (ii) (figs. 21–22) the continuity of the laryngeal with the pharyngeal epithelium extends from the 2nd to the 1st gill-clefts, i.e. is only in the 1st branchial and hyoid segments. The primordium of the laryngeal muscles extends from the 3rd to mid-way between the 2nd and 1st gill-clefts.

In an embryo of 3 cm. the condition of the laryngeal skeleton and laryngeal muscles is identical with that in a 6 cm. embryo, except that chondrification has not taken place.

In a 6 cm. embryo (figs. 23–27) the larynx is raised in a median projection

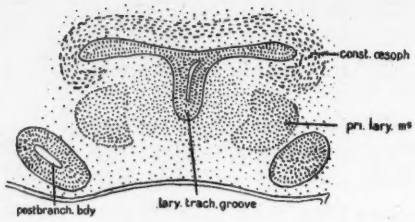
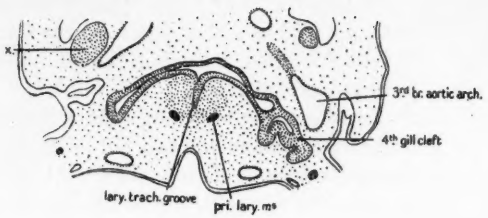


Fig. 7.



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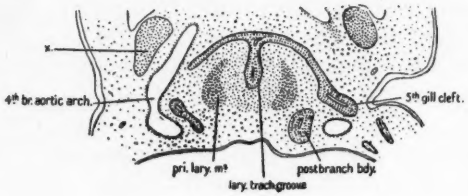

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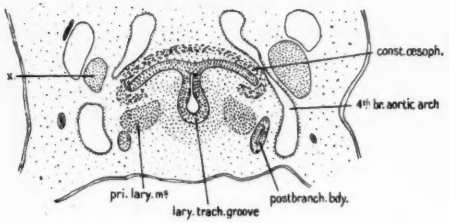

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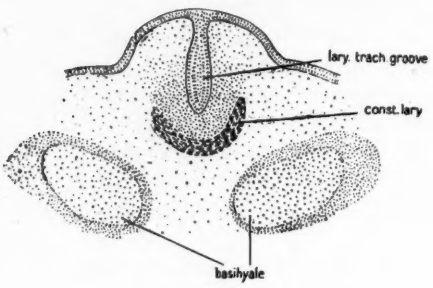

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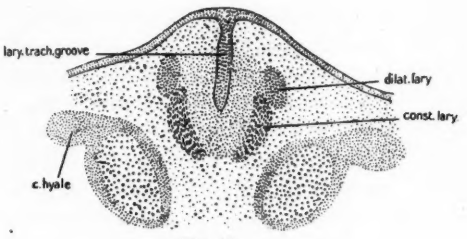

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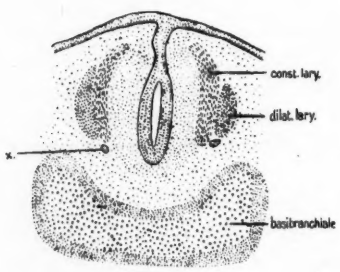

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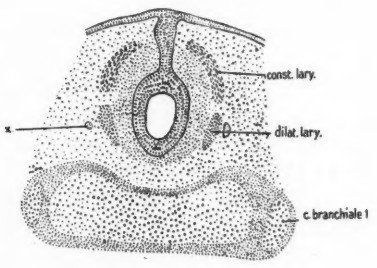

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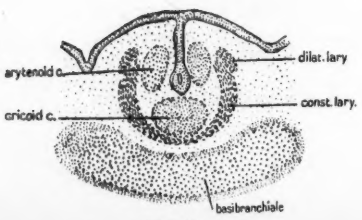

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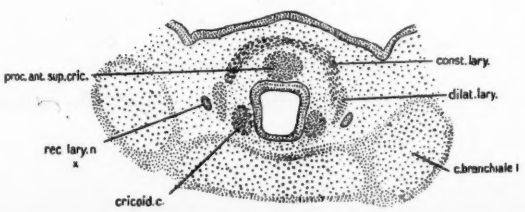

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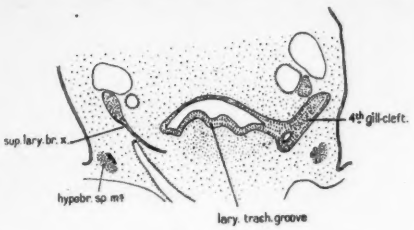

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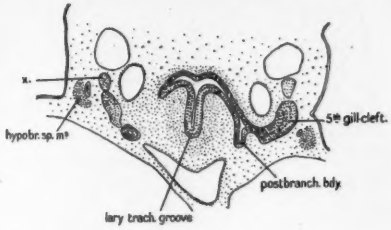

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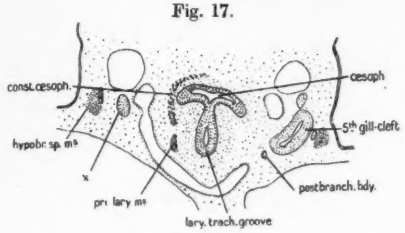

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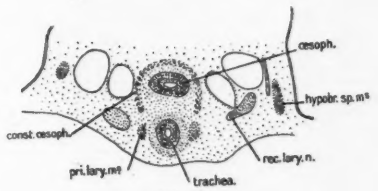

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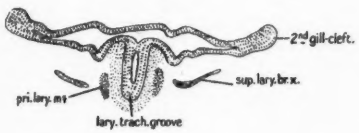
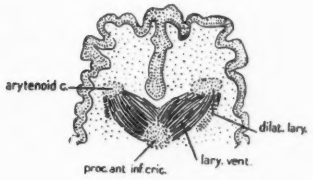


Fig. 21.

Fig. 22.



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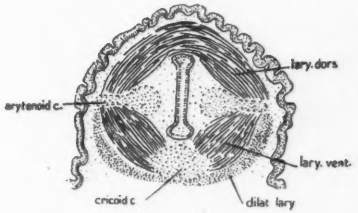

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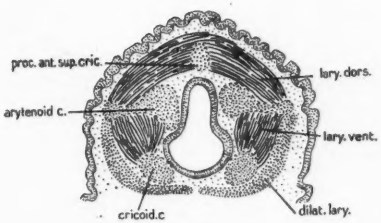

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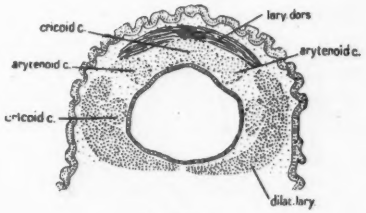


Fig. 26.

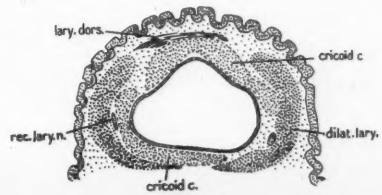


Fig 27.

of the floor of the mouth overlying the tongue. The laryngeal and tracheal skeleton forms a continuous whole and is chondrified. The cricoid has median superior and inferior processes projecting from its front edge. The arytenoids are continuous with the cricoid. The primordium of the laryngeal muscles has separated into the Laryngei dorsalis and ventralis and the Dilatator. The Laryngeus dorsalis arises partly from the dorsal surface of the cricoid and from its anterior superior process and is partly continuous with its fellow across the middle line without any raphé; it is inserted into the dorsal surface of the arytenoid. The Laryngeus ventralis arises from the sloping upper edge of the cricoid and from its anterior inferior process; it is inserted into the ventral surface of the arytenoid. The Dilatator arises from the side of the trachea and from the cricoid, passes forwards and slightly upwards and is inserted into the external edge of the arytenoid.

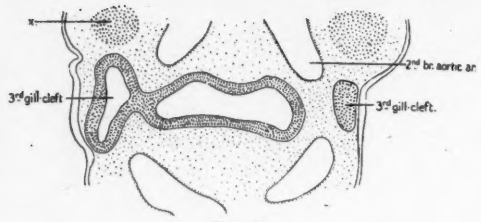
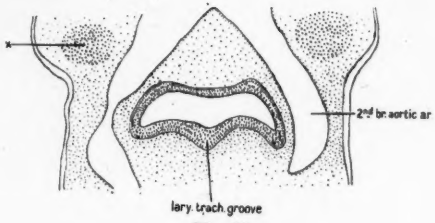


Fig. 28.



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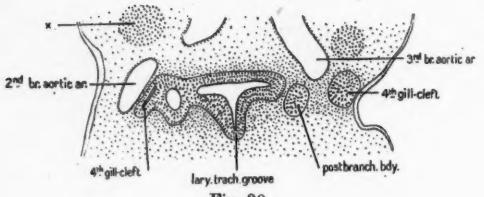

Fig. 30.

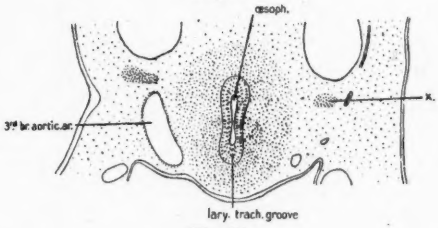

Fig. 31.

Birds. Weber and Buvignier stated that in the duck the primordia of the lungs develop as paired ventro-lateral diverticula of the oesophagus, and the laryngo-tracheal canal later, as a median ventral groove of the oesophageal wall; in the fowl the pulmonary and laryngo-tracheal primordia develop simultaneously.

This was confirmed by Rösler, who also showed that in the sparrow, goose, swallow and pee-wit, the primordia of the lungs develop before the primordium of the laryngo-tracheal canal.

These observers did not investigate the forward extension of the larynx into the pharynx.

In a 3·1/2 day embryo of Gallus (figs. 28–31) the tracheo-laryngeal groove extends from 150 μ behind the 4th gill-clefts to a little in front of it. Dense mesenchyme surrounds the oesophagus and tracheo-laryngeal groove.

In a 4 day embryo (figs. 32–35) the anterior-posterior limits of the tracheo-laryngeal groove are the same; the groove is a little deeper in front of the 4th gill-clefts. The primordium of the Constrictor oesophagi and laryngeal muscles is present as a horse-shoe shaped mass arching over the oesophagus and tracheo-laryngeal groove.

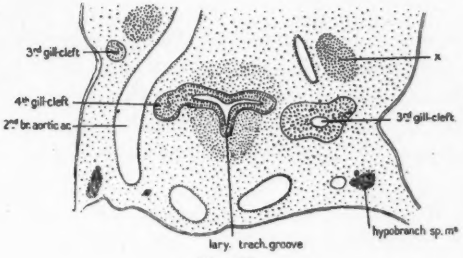

Fig. 32.

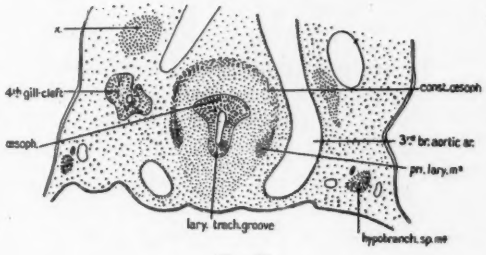

Fig. 33.

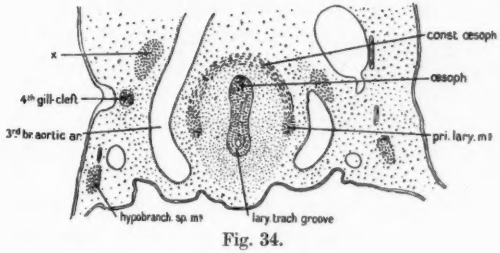

Fig. 34.

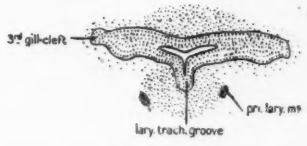

Fig. 36.

Fig. 37.

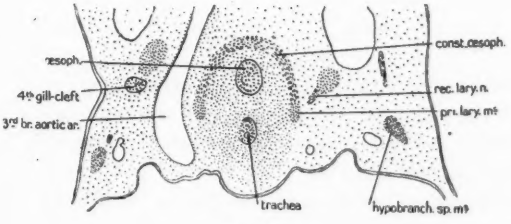

Fig. 35.

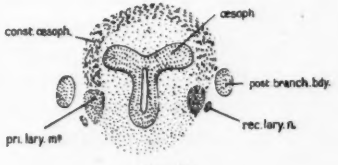

Fig. 38.

In a 5 day embryo (figs. 36–38) the tracheo-laryngeal groove extends from 170 μ behind the 4th gill-clefts to the level of the 3rd gill-clefts. The primordium of the laryngeal muscles has separated, on each side, from the ventral edge of the Constrictor oesophagi; it extends from 140 μ behind the 4th gill-clefts to the level of the 3rd gill-clefts. The recurrent laryngeal nerve lies on its outer side.

In a 6 day embryo (figs. 39–41) the tracheo-laryngeal groove is continuous solely with the pharyngeal epithelium, extending from just in front of the 4th gill-clefts. The lumen of the trachea extends into the ventral part of the larynx. The primordium of the laryngeal muscles extends from 160 μ behind the 4th gill-clefts to the level of the 3rd gill-clefts. In front of the 4th gill-clefts it is broader and thicker than it is behind, and approaches its fellow ventrally.

In a 7 day embryo (figs. 42–44) the primordium of the laryngeal muscles has separated into the (lateral half of) Constrictor laryngis and Dilatator laryngis. The former is obliquely situated and meets its fellow dorsally and ventrally.

In a 10 day embryo (figs. 45–47) the primordia, not yet chondrified, of the cricoid, procricoid, and arytenoid, cartilages are distinguishable in the dense mesenchyme surrounding the larynx.

The above described phenomena in Sauropsida can be summarised as follows. The tracheal and laryngeal epithelium is formed, from behind forwards, as a median groove in the floor of the oesophagus and pharynx. In Chrysemys and Gallus the infolding extends forwards into the last branchial segment—the 3rd branchial in Chrysemys and the 2nd branchial in Gallus. In Tropidonotus, probably in relation with the secondary form of the tongue, it extends into the hyoid segment. The trachea is constricted off from the oesophagus, from behind forwards. In the laryngeal region the walls of the groove come together, and the lumen is afterwards established, in continuity with that of the trachea, from behind forwards. The aditus opens, much later, by separation of the lips of the groove.

The laryngeal musculature, on either side of the tracheal groove, is formed by separation of the ventral edge of the ∩-shaped primordium of the Constrictor oesophagi. It migrates forwards into the branchial s. pharyngeal region. The recurrent laryngeal nerve grows forwards concurrently. The muscle primordium separates, in Chrysemys and Gallus, into the lateral half of the Constrictor laryngis and Dilatator laryngis; in Tropidonotus into the Laryngei and Dilatator.

The laryngeal and tracheal cartilages are developed by chondrification in a thick cellular sheath which develops round the larynx and trachea. In Chrysemys and Gallus the arytenoids become separate structures, in Tropidonotus they remain in continuity with the cricoid.

On the primitive form of the laryngeal muscles in Sauropsida. Göppert stated that in Tropidonotus natrix and Coronella laevis Laryngei dorsalis and ventralis are present, that in Crocodilus biporcatus the Constrictor consists anteriorly and posteriorly of sphincter fibres and in the middle of Laryngei, and that in Midas and Sphargis coriacea whilst the main mass is a sphincter there is anteriorly a Laryngeus ventralis.

He concluded from the above that the primitive form in Reptiles is Laryngei and that a Constrictor is secondary. (He had previously come to the same opinion in Amphibia.)

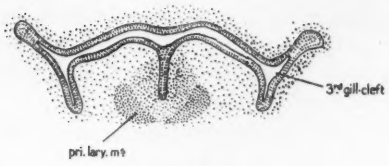

Fig. 39.

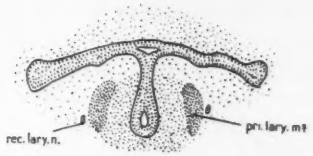

Fig. 40.

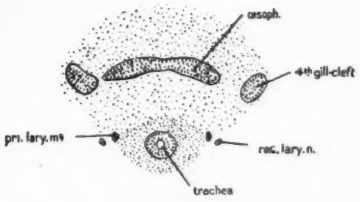

Fig. 41.

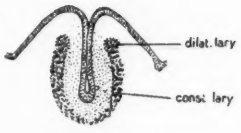

Fig. 42.

Fig. 43.

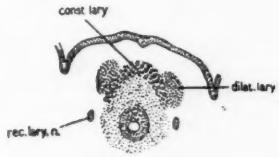

Fig. 44.

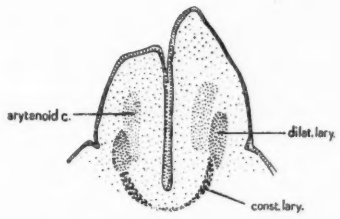

Fig. 45.

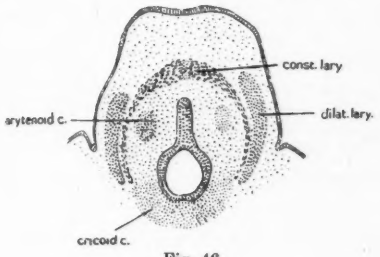

Fig. 46.

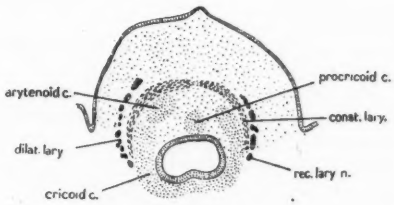

Fig. 47.

This, however, is by no means certain, for in Tropidonotus (vide figs. 24–27) the dorsal musculature is in part a Constrictor, in Chrysemys and Gallus the developmental stages show no trace of the Constrictor being formed by fusion of Laryngei. Hoffman states (in Bronn) that in Reptiles the usual condition is a Constrictor, and Gadow that the condition in Birds is a Constrictor.

These facts suggest that the ancestral Sauropsidan condition was a Dilatator and a Constrictor laryngis.

Some further considerations on the laryngeal muscles are deferred to a later paper.

I have to thank the Bristol University Colston Society for defraying the expense of the above described investigation.

July 11, 1919.

LIST OF FIGURES

The figures are taken from serial transverse sections—in all cases the lowest number denotes the most anterior section.

Chrysemys.

Figs. 1–3 through an embryo 6 mm. long. Fig. 1 through the 5th gill-clefts, figs. 2 and 3 behind them.

Figs. 4–6 through an embryo 7 mm. long. Fig. 4 through the 4th gill-clefts, fig. 5 through the 5th gill-clefts, fig. 6 behind them.

Fig. 7 through an embryo 8 mm. long behind the 5th gill-clefts.

Figs. 8–10 through an embryo 9 mm. long. Fig. 8 through the 4th gill-clefts, fig. 9 through the 5th gill-clefts, fig. 10 behind them.

Figs. 11–14 through an embryo 12 mm. crown-rump length.

Figs. 15–16 through an embryo 15 mm. crown-rump length.

Tropidonotus.

Figs. 17–20 through an embryo, stage (i): fig. 17 through the 4th gill-clefts, fig. 18 through the 5th gill-clefts, figs. 19 and 20 behind them.

Figs. 21–22 through an embryo, stage (ii): fig. 21 through the 2nd gill-clefts, fig. 22 between the 2nd and 3rd gill-clefts.

Figs. 23–27 through an embryo 6 cm. long.

Gallus.

Figs. 28–31 through an embryo of 3·1/2 days' incubation; fig. 28 through the 3rd gill-clefts, fig. 29 between the 3rd and 4th gill-clefts, fig. 30 through the 4th gill-clefts, fig. 31 behind them.

Figs. 32–35 through an embryo of 4 days' incubation; fig. 32 through the 4th gill-clefts, figs. 33–35 behind them.

Figs. 36–38 through an embryo of 5 days' incubation; fig. 36 through the 3rd gill-clefts, fig. 37 through the 4th gill-clefts, fig. 38 behind them.

Figs. 39–41 through an embryo of 6 days' incubation; fig. 39 through the 3rd gill-clefts, fig. 40 between the 3rd and 4th gill-clefts, fig. 41 through the 4th gill-clefts.

Figs. 42–44 through an embryo of 7 days' incubation.

Figs. 45–47 through an embryo of 10 days' incubation.

ABBREVIATIONS

arytenoid c.	arytenoid cartilage
br. aortic ar.	branchial aortic arch
const. lary.	constrictor laryngis
const. oesoph.	constrictor oesophagi
c. branchiale i	cornu branchiale i
c. hyale	cornu hyale
cricoid c.	cricoid cartilage
dilat. lary.	dilatator laryngis
dor. aor.	dorsal aorta
hypobr. sp. ms.	primordium of hypobranchial spinal muscles
lary. dors.	laryngeus dorsalis
lary. vent.	laryngeus ventralis
oesoph.	oesophagus
procricoid c.	procricoid cartilage
proc. ant. inf. cric.	processus anterior inferior of cricoid cartilage
proc. ant. sup. cric.	processus anterior superior of cricoid cartilage
procricoid c.	procricoid cartilage
postbranch. bdy.	postbranchial body
pri. lary. ms.	primordium of laryngeal muscles
rec. lary. n.	recurrent laryngeal nerve
sup. lary. br. x.	superior laryngeal branch of vagus
lary. trach. groove	laryngo-tracheal groove
trans. groove	transverse groove
x.	vagus nerve

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PERSISTENT FORAMEN PRIMUM, WITH REMARKS ON THE NATURE AND CLINICAL PHYSIOLOGY OF THE CONDITION

By ALEXANDER BLACKHALL-MORISON, M.D., F.R.C.P.

M. G., 43 years of age, married, and the mother of five healthy children, was admitted on July 15th, 1918, under my care at Mount Vernon Hospital at Northwood. She was stated to have had rheumatic fever when a child seven years old, and for twelve months prior to admission to have suffered from a degree of dyspnoea with palpitation of the heart and some swelling of the feet.

On examination, the apex beat was found to be in the sixth left interspace five inches from mid-sternum in the dorsal position. On right decubitus the apex beat was in the fifth left space three inches from the mid-sternal line. That is, there was no symphysis cordis. The left upper ventricular dulness lying on the back was at the third left rib and the right cardiac dulness at the left edge of the sternum. There was systolic pulsation in the suprasternal fossa and some fulness and pulsation in the right external jugular vein.

There was a systolic bruit of rather high pitch, loudest in a space three inches from mid-sternum to the apex beat. It was traceable to the left and distinctly audible in the left paravertebral groove and also, but less so, in the right paravertebral groove. The aortic valves were heard to close perfectly in diastole and there was no reduplication of the second sound of the heart. The closure of the pulmonary arterial valves was palpable. While, therefore, I had some doubt as to the precise character of the lesion, I was inclined to regard it as one permitting reflux through the mitral valve. I think I was justified in doing so, for reasons which I need not detail here, but I was, nevertheless, wrong, as the conditions found after death proved. The pulse rate at this period was 84 to 96 and its rhythm regular.

Examined later, the physical signs remained much the same, but the area of cardiac dulness was increased, and the pulse rate was accelerated and it had become irregular. The patient had, at this period, a long sustained attack of paroxysmal tachycardia, when the pulse rate reached 198 in the minute. There was passive congestion of both lungs and enlargement of the liver with signs of commencing stasis in the systemic venous system. From this grave condition the patient partially recovered; the paroxysmal tachycardia subsided, the pulse rate falling to 92–112; she was able to leave her bed and to sit on a reclining chair and expressed herself as feeling better. But the heart

had entered on the last phase of progressive failure. There was increasing evidence of anasarca, of effusion into the serous cavities in chest and abdomen, and of albuminuria. She became ever more restless and sleepless and finally died collapsed and comatose on Oct. 15th, 1918.

The post-mortem examination was made by Dr Kinton, Resident Superintendent of the Hospital, assisted by Dr R. J. Cyriax, the House Physician. The heart after removal from the body was placed in weak formalin solution for examination later by myself, and I am indebted to Dr Cyriax for the drawing of the conditions found, which I now exhibit.

The general data discovered, bearing upon the condition of the heart, which need be mentioned were, that there was serous effusion into the pleurae and peritoneal cavity and that the pericardial sac contained three ounces of fluid instead of the normal drachm or two; the liver was enlarged, weighing 61 ounces, and showed the usual passive congestion of progressive cardiac failure, as did the lungs and the kidneys. The latter weighed six and five ounces respectively and their capsules stripped off easily. The spleen weighed six ounces.

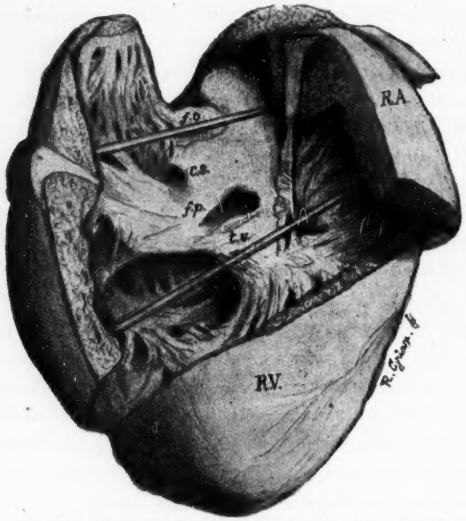
The condition of the heart is as follows: It weighs after evacuation of blood and hardening in formalin solution, one pound seven ounces, that is, it has at least twice the average weight of the normal female heart. On the anterior surface of the left ventricle, near its apex, there is a milk spot measuring 2·5 by 3 cms.

The right auricle is markedly hypertrophied. The auricular wall near the auriculo-ventricular junction measures 1·5 cms., that is, about half an inch. The musculi pectinati, crista terminalis and other muscular markings are well defined. The foramen ovale is large and completely closed. The entrances of the inferior and superior venae cavae are normal and the muscular anterior wall of the superior caval entrance powerfully hypertrophied. The orifice of the *coronary sinus* is rather smaller than usual.

Below and anterior to the coronary sinus and immediately above the insertion of the septal cusp of the tricuspid valve there is *an orifice* large enough to admit the forefinger and passing directly into the left auricle. The attachment of the septal cusp partly by very short cordae tendinnae and chiefly by direct adhesion to the moderator band in the right ventricle is extremely short and tight. It could have exercised little valvular function. The anterior cusp appears to be normal and the posterior rather smaller than usual. The atrio-ventricular orifice admitted three fingers and from its anatomical condition probably permitted regurgitation into the auricle. All measurements it will be noted are after immersion in formalin solution and, therefore, are probably smaller than in life.

The *right ventricle* is powerfully hypertrophied, its wall having a diameter of 2 cms. near the auriculo-ventricular junction and of 1·5 cms. about the middle of the chamber. The *moderator band* is well developed and the columnae carneae and trabeculae generally, powerfully hypertrophied. The valves of

the pulmonary artery are normal, competent and rather capacious. The pulmonary artery itself is dilated and its wall thicker than usual but there is no atheroma. The *left auricle* is normal and in no way hypertrophied. The left auriculo-ventricular orifice admits two fingers from above. The finger passed through the persistent foramen primum, goes directly into the left atrio-ventricular orifice. The left ventricle although well developed muscularly is not markedly hypertrophied. Its walls measure at thickest 2 cms., the cavity is not dilated and the papillary muscles and trabeculae generally are not hypertrophied. The *mitral cusps* are well formed and apparently competent. The *aorta* is practically free from atheroma, rather below the average



Persistent Foramen Primum showing interior of right auricle and ventricle. The walls are held apart by glass rods. ½ nat. size. *R.A.* right auricle; *f.o.* foramen ovale; *c.s.* coronary sinus; *f.p.* foramen primum; *t.v.* tricuspid valve; *R.V.* right ventricle.

in size and its walls are thin. The three semilunar cusps are normal and the posterior one attached to a deep sinus of Valsalva. There are two patent coronary arteries. The interventricular septum is perfect.

Remarks. As the interauricular curtain (septum primum) is dropped, in embryo, towards the endothelial cushions which mark the line of the auriculo-ventricular valves, in certain cases, the growth of the septum is arrested and a communication between the auricles remains, which under normal circumstances would not be present. A section of the arrested curtain, examined microscopically, shows it to be a true arrest of development and not the result of any foetal endocarditis (Morison, *Journ. of Anat. and Phys.* vol. XLVII. p. 467).

This communication may be large or small. In a case which I showed before this Society in 1913 (*Journ. of Anat. and Phys. loc. cit.*) it was very large and incompatible with any length of life. The child, a male, died when six months old, after having been under observation for one month. It showed after death, collapsed lung with scattered patches of induration, which were probably atelectatic, although they were not examined microscopically—a persistent foetal state. There was hypertrophy of the right auricle and ventricle, none of the left auricle and little of the left ventricle and, as in the present instance, a small coronary sinal orifice. The bruit observed clinically was also systolic and apical but heard best in the back.

Professor Keith remarks, in his lectures on Malformations of the Heart (*Lancet*, vol. II. 1909, p. 435) that this defect "is not necessarily accompanied by grave disturbance of the heart." The defect is, however, very apt to be associated with some abnormality of the auriculo-ventricular valves as is readily conceivable from the position and nature of the defect. Dr Maude Abbot (*Osler and McCrea's System of Med.* vol. IV. p. 357, 2nd edition) relates that, in five out of seven cases reported by Rokitansky, the anterior segment of the mitral valve was "cleft from its free border to its insertion." In the case which I now show the mitral valve was normal but the septal cusp of the tricuspid valve was, as I have stated, adherent to the moderator band so as to be functionally incompetent.

Although, as in the present case, the bearer of the lesion may live for a considerable period and fulfil the ordinary functions of the human being—in this case the cardiopath as stated had five children and was 43 years of age—I do not know whether any of the cases presenting this defect have been much older. If they have, it will probably be found that the defect had developed in such a manner as to leave the atrio-ventricular orifices well guarded by their valves.

In 1918, I showed before the Society the heart of a man with a much stenosed pulmonary arterial orifice, a shrunk right ventricle and a hypertrophied and dilated right auricle. The owner of it died at the age of 72, but in this case, the avenue of relief between the auricles was a largely patent foramen ovale, the septa of the auricles and ventricles being otherwise normally complete. But patency of both the foramen ovale and foramen primum may co-exist (Thomson, *Proc. Anat. Soc.* 1902–3, XXXVI.). The case I now show (Mrs G.'s) also illustrates the secondary pathological changes usually observed in persistent foramen primum, namely, general escape of the left chambers from hypertrophy, some hypoplasia of the aorta, dilatation of the pulmonary artery, marked hypertrophy of the right chambers and, as I have pointed out, a certain smallness of the orifice of the coronary sinus.

To a clinician, all such conditions, primary and secondary, are of interest, as indicating where the strain of conducting the circulation has been most felt by the heart. As these points are a matter of morbid physiology they may be mentioned here. I should myself feel disposed to modify the conclusion

expressed by Professor Keith already quoted, by maintaining that the defect "is not necessarily accompanied by grave disturbance of the heart," but only for a time, and that it always ultimately causes grave disturbance and is incompatible with length of life in proportion to the degree in which the atrio-ventricular valvular apparatus is involved in the genesis of the defect.

Clinically the rhythm and situation of the bruit audible in these cases is of interest. In both my cases the bruit was systolic in time, mainly apical in situation and audible (unlike the presystolic bruit of mitral stenosis) posteriorly as well as anteriorly. Without atrio-ventricular valvular defect or incompetency, one would expect any bruit present in persistent *foramen primum* to be presystolic, that is, auricular systolic in time. But if this time of the bruit be observed in such a case, it will probably be found as I have stated, that it is audible posteriorly as well as anteriorly. It is very desirable in all cases of congenital heart disease, if any bruit be present, that it should be very carefully noted as to character, rhythm and localisation, for diagnostic purposes.

It is evident from what has been said as to the condition of the chambers in the left or arterial heart that the strain of the circulation in these cases is chiefly upon the dextral chambers.

The hypoplasia of the aorta, taken in connection with the dilatation of the pulmonary artery, in the absence of left auricular dilatation and hypertrophy, together with the lack or small degree of hypertrophy of the left ventricle, points to a deficiency in the normal plenitude and permeability of the pulmonary circulation. This is probably due in a measure to a persistence of the foetal condition, in so far as the defect diminishes the aspirative and propulsive force of respiration. In the completely foetal condition, the extent of the pulmonary circulation being at a minimum and the transmission of the blood to the arterial system secured by adequate channels, no dilatation of the pulmonary artery occurs, but the right chambers preponderate in power and in muscular development over the left.

In persistent foramen primum, on the other hand, extra uterum, the lungs are in action, and a large quantity of blood *does* reach the pulmonary circulation but without the full aid of the aspirative force resident in the normally constituted left heart. With the closure or the practical closure of the ductus arteriosus under these circumstances, the powerful right ventricle, while it fails to drive sufficient blood through the lungs into the left heart, tends, in diastole, to retain blood in the pulmonary artery and its main branches. Hence their dilatation and the baggy valves which guard that vessel. The incomplete plenitude of left cardiac blood thus serves to explain the total absence of left auricular and the comparative absence of left ventricular hypertrophy in these cases and likewise the hypoplasia of the thin walled aorta met with in many such instances. That very considerable hypertrophy of some parts of the organ is, nevertheless, present is proved by the notable increase in the weight of the organ and this, in the absence of vascular or renal

conditions, is calculated to induce hypertrophy of the cardiac muscle from other causes than the purely mechanical cardiac defect.

Finally, it may be stated that the bearer of the congenital defects (foramen primum and abnormal tricuspid valve) in the present instance, although stated to have suffered from rheumatic fever as a child, showed no evidence in endocardium or pericardium of consequences of that disease. The changes, therefore, noted in the organ were a result of the congenital anatomical states described and the modified physiological actions which resulted from them. Here again, then, as in other cases I have shown to this Society, the importance of integrity of the valvular apparatus, for an efficient and easy conduct of the circulation through the heart, is manifest.

In Memoriam

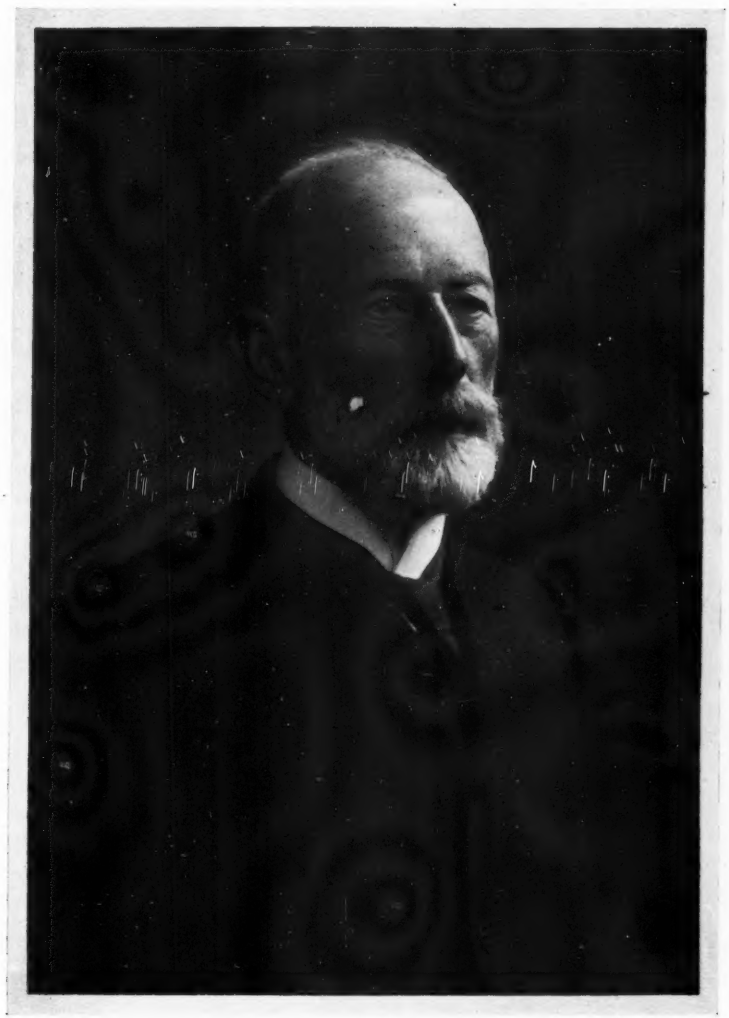
Professor ALEXANDER MACALISTER, M.D., F.R.S., etc.
1844—1919

One of the earliest and strongest links in the history of the *Journal of Anatomy* and of the Anatomical Society has been broken by the deeply lamented death of Alexander Macalister.

Ever active in promoting the interests of the *Journal* his name is appended to an interesting paper on muscular anomalies appearing in the first volume and its earlier pages are rich in his learned and thoughtful contributions. In 1898 he joined the editorial staff becoming acting editor in 1910. As acting editor he was indefatigable, reading every paper submitted to him with the most scrupulous and meticulous care and earning the gratitude of many a contributor for advice, information and help. He was always of the opinion that the *Journal* should be well illustrated and spared no trouble and expense to this end.

The Anatomical Society must regard Macalister as one of its parents. It was initiated in 1887 as the result of a series of week-end conferences held at Cambridge in 1886 between Humphry, Lockwood and himself. For years he was a constant attendant at its meetings, took an active part in its proceedings, and was its President in 1898. In 1889 he drew the attention of the Society to the desirability of a scheme for coordinated research. The resulting Committee of Collective Investigation accumulated a considerable amount of valuable information but came to an untimely end. He always held the view that the *Journal* should be under the direct management of the Society and it was largely due to his warm advocacy and unselfish interest that this was brought about last year.

The story of Macalister's early life reads more like a romance than sober fact. He was born in 1844 in Dublin, whither his father, Robert Macalister of Paisley, had migrated to succeed Will Carleton, the Irish novelist, as Secretary to the Sunday School Society of Ireland. Robert Macalister, blessed with a large family and a slender purse, destined his son Alexander to a business calling. As a school-boy he developed the most diligent habits and early displayed a love for biological study spending all his available leisure time in the Glasnevin Botanic Gardens. There he attracted the attention and interest of the Curator who recognising that he was no ordinary boy persuaded his father to let him study Science. Consequent on special recommendation



Phot. by *Lafayette*

PROFESSOR ALEXANDER MACALISTER,

M.A., M.D., LL.D., D.SC., F.S.A., F.R.S.

he was allowed to commence his medical studies at the Royal College of Surgeons of Ireland at the incredibly early age of 14. From this point his progress was meteoric. He was appointed Demonstrator of Anatomy at the College at 16 and at 17 obtained the double qualification. Entering Trinity College Dublin, he was elected Professor of Zoology at the University of Dublin while still an undergraduate, and was precluded from proceeding to an honours degree in Science, the would-be examinee being an examiner. Could anyone imagine a more Gilbertian situation? In addition to his professorial duties he lectured on Botany, Geology, Astronomy and I know not how many other sciences at Alexandra College, Dublin. In 1877 he was appointed Professor of Anatomy and Chirurgery at Trinity College, Dublin and Surgeon to Sir Patrick Dun's Hospital. Six years later he succeeded Humphry in the Chair of Anatomy at Cambridge, where he laboured incessantly and with the utmost devotion for 36 years, for the same length of time as Turner held the corresponding chair at Edinburgh.

In his early years Macalister was a most prolific writer—text-books, monographs and papers following one another with startling rapidity. Special attention may be recalled to his "Observations of Muscular Anomalies," read in abstract before the Royal Irish Academy in January 1871, and compiled during a Summer recess in the previous year. A complete survey of the variations affecting the whole muscular system of man it was a most amazing piece of work and a wonderful tribute to his immense patience and untiring energy. Careful study reveals the fact that not only did he collate everything that had ever been written on the subject but 50 per cent. or more of the material which he presents is the result of his own personal observations —observations which having stood the test of years and been confirmed again and again have become classical. He confesses to having taken part in the dissection of over 690 subjects, while the tedious and intricate dissections necessary to furnish him with such numerous examples from the face, scalp, pharynx, soft palate, etc. transcend the imagination. This is the work of a young man of 26, immersed in professorial duties and busily engaged in laying the foundations of two large treatises on Zoology to appear a year or two later.

His great text-book of Anatomy, great in more senses than one, was published in 1889. There are few anatomists but owe a debt and that a considerable one to its pages. Utterly unlike anything that has appeared before or since it was no mere compilation but original in thought and treatment, replete with personal observation and an index of the man himself. If fault it had it was that of compression. Macalister had so much to tell and the confines of a large text-book were for him so limited that he was forced to prune, curtail and abbreviate at every step. The wonder is that no second edition ever appeared but therein lies a tragedy. An interleaved copy of the book was always lying on his table and in this he daily added new facts, observations and reflections until in a few years time it was full to overflowing. One day it disappeared never to be found again. Its loss was met with characteris-

tic and cheerful fortitude, but it was a blow from which he never recovered, and it sealed the fate of a subsequent edition.

Macalister was wont to give a course of lectures on the historical aspects of Anatomy in the Summer term at Cambridge. Choosing a new subject year by year he covered a vast field, giving his critical acumen full play, displaying a wonderful power of broad survey and discovering links hitherto unsuspected. Most especially is it to be regretted that he never fulfilled the hope expressed in the preface of his text-book to write a "detailed history of the progress of Anatomical discovery." No one in the world was better equipped for the task. Exploring anatomical literature had long become a habit and he had spent much of his life in the University Library at Cambridge, rich beyond compare in the works of the earlier anatomists. He gives us some foretastes of what might have been in his "Memoir of James Macartney," "A Sketch of the History of Anatomy in Ireland," "The History of the Study of Anatomy in Cambridge" and "Archaeologia Anatomica" which appeared from time to time in the *Journal of Anatomy*, and which though unsigned were the products of his pen.

The eminent service Macalister rendered in elevating Anatomy from a mechanical study into a living science is perhaps insufficiently realised at the present day. No bare fact ever presented itself to him but it set him thinking of the part it played in the mystery of life and the problem of existence. This may not be apparent in many of his writings, but was pre-eminently so in his teaching and influence. An exception to this general statement is afforded by "Some Morphological Lessons taught by Human Variations," a Robert Boyle lecture delivered at Oxford in 1894. Therein he sets forth in masterly fashion the deductions he draws from a study of variations to the garnering of which he had always been irresistibly attracted.

Endowed with a marvellous and orderly memory, infallible and almost uncanny in its tenacity for minute detail, Macalister had the most astounding facility for accumulating information and facts not only from books but at first hand from dissecting room and museum. He would devote endless pains and infinite patience to obtaining and noting new facts, but once acquired they seemed to lose further interest and he could rarely be prevailed upon to publish them. Not a tithe of them appear in his published writings, some lie stored in countless note-books, but many alas! are gone with him. In the disposal of his stores he was generosity itself, they were offered freely and openly to one and all to make what use of them they liked.

His lectures were an intellectual treat and are held as most valued recollections by all who were privileged to listen to them. His facile eloquence, lightened by occasional flashes of quaint dry humour, would at times fascinate and almost mesmerise his hearers. Following no tradition, shackled by no exigencies of examination, a rich spring of anatomical knowledge, ornate with morphological illustration and historical interlude, flowed out in a quiet but inspiring stream.

No professor ever spent so many hours in the dissecting room. He revelled in the practice of his art and was the neatest and most rapid exponent I have ever seen, devoting the same scrupulous care to the most trivial display as to the most intricate manipulation.

To do adequate justice to Macalister's great learning and scholarship is an impossible task. Although he knew more about the anatomy of the human body than any man living, anatomy after all was but a small part of his mental equipment. He was an able mathematician and familiar with many languages both living and dead. In Archaeology, Zoology, Egyptology, Theology, Biblical history, to mention but some of the subjects which aroused his interest, he was an inexhaustible mine of knowledge. In discussion on many and diverse subjects, he was conspicuously the authority and source of accurate information, often to the confusion of the expert. His indefatigable industry and insatiable thirst for knowledge persisted throughout life and in these respects he never grew old.

Despite his great attainments he had the most kindly and gentle disposition, was ever considerate for the opinions and feelings of others and endeared himself to all who met him. It was an inestimable privilege to have known him and his loss leaves a blank which can never be filled.

E. B.-S.

REVIEWS

THE PERIPHERAL NERVES

THE aid of the anatomist—in many places his personal aid—has been much sought by the surgeon in the extensive and detailed knowledge of the peripheral nervous system which has been demanded of him during recent years. It is with considerable interest, therefore, though mingled with a sense of the personal loss, that one turns to the volume on this subject by the late Professor Paterson[1], knowing that it has been written by an anatomist of authority and by one with the experience of the R.A.M.C. officer. His book is founded, even at first sight, on a wide basis, since by an appeal to the general morphology and development of nerves he has aimed primarily at an explanation of the principles which govern the facts of peripheral nerve distribution. One may doubt the value of, or even disagree with the views expressed in, for example, the chapter on "The Nature of the Limbs," but that Professor Paterson was correct in adopting the broader plan will be felt at once, even by those who may be introduced for the first time to morphological concepts, not merely from the educative point of view, but, for instance, as affording the only assistance towards understanding the "plan" of the common variations of nerves which otherwise remain a seemingly uncalled-for mystery. He has incorporated in his general account of the nerves, in a way which will be recognised as peculiarly his own, many of his own deductions on the critical questions of the subject, and the trained observer is well seen in his notes on the vascularity of the ends of the severed nerves. The book does not aim at being encyclopaedic nor claim to be a book of reference, but as a general statement of the anatomy of the peripheral nervous system by a recognised authority on that subject, it is indeed worthy of the study of those whose work requires the knowledge it contains, and whose inclinations lead them to seek more than the mere summation of fact. The anatomist will pay it the attention it merits from his regard for the writer.

The other book before us on this subject—Dr Whittaker's revisal of the late Professor Hughes' *Handbook of the Nerves of the Body*[2]—is a concise summary of the main facts of the distribution of the peripheral nerves and the sympathetic system, and should serve excellently as a preliminary statement for one revising the empiricism of these subjects. It is, however, the pure hard fact of systematic anatomy, and, though not detracting from its usefulness on that account, is essentially a summarised extract of any good anatomy textbook. The plates are purely diagrammatic, and as such are of assistance to the text. They are well reproduced.

[1] *The Anatomy of the Peripheral Nerves.* Prof. A. M. Paterson, M.D., F.R.C.S. Henry Frowde and Messrs Hodder and Stoughton. pp. vi + 165. 12*s.* 6*d.* net.

[2] *Nerves of the Human Body.* C. R. Whittaker, F.R.C.S. (Ed.) E. and S. Livingstone, Edinburgh. pp. viii + 72. 12 plates. 3*s.* 6*d.* net.